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Indicated for the treatment of modified Outerbridge Grade III and Grade IV cartilage lesions in the knee. CE marked and regulated as a Class III medical device in Europe.

INSTRUCT – a unique approach to cartilage repair in the knee
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INDEX

Presidents’ Voice 5
Past President’s Reflections 7
News from the ICRS Office 10
ICRS Web & Social Media Performance Unveiled 10
New ICRS “Social Media Evangelists” 12
Welcome to 52 New Members 13
The ICRS Office on the Road 13
Message to our Industry Partners 14
Report from Past ICRS Meetings 14
Report ICRS/Zimmer Scholarship 17
Event Calendar 18
Upcoming ICRS Educational Events 19
Call for Abstracts – ICRS 2015 – Chicago, USA 21
ICRS Journal Club 23
Interview with Robin Poole 24
Do’s and Don’ts in the Laboratory 30
LONG LIVE KNEES

CHONDROCELECT PRESCRIBING INFORMATION

NAME OF THE MEDICINAL PRODUCT: ChondroCelect 10,000 cells/microlitre implantation suspension.

QUALITATIVE AND QUANTITATIVE COMPOSITION: General description: Characterised viable autologous cartilage cells expanded ex vivo expressing specific marker proteins.

Qualitative and quantitative composition: Each vial of product contains 4 million autologous human cartilage cells in 0.4 ml cell suspension, corresponding to a concentration of 10,000 cells/microlitre.

Pharmaceutical form: Implantation suspension. Before re-suspension the cells are settled to the bottom of the container forming an off-white layer and the excipient is a clear colourless liquid.

Therapeutic indications: Repair of single symptomatic cartilage defects of the femoral condyle of the knee (International Cartilage Repair Society [ICRS] grade III or IV) in adults. Concomitant asymptomatic cartilage lesions (ICRS grade I or II) might be present. Demonstration of efficacy is based on a randomised controlled trial evaluating the efficacy of ChondroCelect in patients with lesions between 1-5cm².

Posology and method of administration: ChondroCelect must be administered by an appropriately qualified surgeon and is restricted to hospital use only. ChondroCelect is solely intended for autologous use and should be administered in conjunction with debridement (preparation of the defect bed), a physical seal of the lesion (placement of a biological membrane, preferentially a collagen membrane) and rehabilitation. Posology: The amount of cells to be administered is dependent on the size (surface in cm²) of the cartilage defect. Each vial contains an individual treatment dose with sufficient number of cells to treat the pre-defined lesion size, as measured at biopsy procurement. The recommended dose of ChondroCelect is 0.8 to 1 million cells/cm², corresponding with 80 to 100 microlitre of product/cm² of defect. Method of administration: ChondroCelect is intended solely for use in autologous cartilage repair and is administered to patients in an Autologous Chondrocyte Implantation procedure (ACI). The implantation should be followed by an appropriate rehabilitation schedule for approximately one year, as recommended by the physician.

Contraindications: Hypersensitivity to any of the excipients or to bovine serum. ChondroCelect must not be used in case of advanced osteoarthritis of the knee.

Undesirable effects: In a randomized, controlled study in the target population, 51 patients were treated with ChondroCelect. In these patients, a periosteal flap was used to secure the implant. Adverse reactions occurred in 78.4% of the patients over a 36-months postoperative follow-up period. The most common adverse reactions were arthralgia (47.1%), cartilage hypertrophy (27.4%), joint crepitation (17.6%) and joint swelling (13.7%). Adverse reactions collected from 370 patients included in a Compassionate Use Program are similar to those reported in the target population. Most of the reported adverse reactions were expected as related to the open-knee surgical procedure. The most frequently occurring reactions reported immediately after surgery include joint swelling, arthralgia and pyrexia. These were generally mild and disappeared in the weeks following surgery. Adverse reactions of special interest: Arthrofibrosis: In the compassionate use patients, a higher incidence of arthrofibrosis and decreased joint range of motion was observed in a subgroup of patients with a patellar lesion (8.2% and 13.1% respectively) compared to non-patellar lesions (0.6% and 2.6% respectively). Cartilage hypertrophy: In the majority of the 370 patients included in the Compassionate Use Program, a collagen membrane instead of a periosteal flap was used to seal the defect. According to current literature the incidence of cartilage hypertrophy can be reduced by using a collagen membrane to cover the lesion site instead of using a periosteal flap (Gooding et al., 2006; Niemeyer et al., 2008). When a collagen membrane was used to seal the lesion site after application of ChondroCelect, the incidence of cartilage hypertrophy was reported to be 1.8% compared to 25% in the randomized, controlled trial alone.

Tigenix NV, Romeinse straat 12/2, B-3001 LEUVEN, Belgium. Medicinal product subject to restricted medical prescription – restricted to hospital use only. Marketing authorisation number: EU/1/09/563/001. 9-2013/V1.
When I write this, it’s travelling season again. All the large societies send invites to their annual or bi-annual meetings – AAOS, ESSKA, EFORT, AOSSM, JOA (no ISA-KOS this year). ... Big and very big conferences offer presentations in 10-15 parallel sessions, a wide variety of topics covering every detail in the field and with industrial exhibits with displays, sometimes worth a single family home. Great places to network and to learn what’s new (or not anymore). Is there still room or need for a society like ICRS – with a narrow focus and a limited market?!

SURE there is!

Smaller focussed meetings allow for greater interaction with the specialists in the field – we can ask what we really want to know. The past Focus Meeting on Stem Cells & Scaffolds in Bologna/Italy 2013 was a benchmark event in cartilage education. The Focus Meeting – The Knee in Zurich, Switzerland was sold out 3 months in advance. So keep a look out for the next ICRS Focus Meetings – Allografts in Brussels/Belgium on Feb 26/27, 2015 and on Subchondral Bone Disorders in September 2015 in Jerusalem/Israel.

Effective networking with all the stakeholders in the field saves time and effort. We all appreciate great presentations, but - hands-on is key; taught and learned at the ICRS Surgical skills course or laboratory course series. This is how we help our patients and advance science. Check out the program and agendas of the next hands-on events; the 5th ICRS Surgical Skills Course to be hold in Larissa/Greece from Oct 23-25, 2014 and the next Laboratory Skills Course, taking place from Oct 27-29, 2014 in Fort Collins/USA. More to come for 2015 in Rosemont/USA, Mexico City and Sao Paolo. Stay tuned!

ICRS can react quickly to visions, ideas, new developments and demands from our customers. The ICRS summit series offers food for thought, outside the box to a selected and dedicated group of clinicians, scientists and industrial partners. Please mark your agenda and apply soon for the 2015 ICRS Summit Meeting – The Aging Cartilage – January 14-17, 2015 in Zermatt/Switzerland.

Yes, there IS room and need for a specialized society like ICRS! We just have to fill the open spaces on a high level. What ICRS discusses now will be presented elsewhere 3 years from now. Let’s keep it that way! Let’s focus! Let’s ICRS!

Chris Erggelet, ICRS President 2013 – 2015

Advancing science & education in cartilage repair worldwide!

**Mark your Agenda!**

ICRS Focus Meeting – The Knee, Zurich – Switzerland
July 3 - 4, 2014 (SOLD OUT)

5th ICRS Surgical Skill Course (Wet-Lab), Larissa – Greece
October 23 – 25, 2014

5th Laboratory Skills Course for Translational Science, Fort Collins – USA
October 27 – 29, 2014

Call For Abstracts – ICRS 2015
Submission Deadline: November 10, 2014

2nd ICRS Summit – The Aging Cartilage, Zermatt – Switzerland
January 14 – 17, 2015

ICRS Focus Meeting – Allografts, Brussels-Belgium
February 26 – 28, 2015

6th ICRS Surgical Skills Congress, Chicago – USA
May 07 – 08 2015

12th ICRS World Congress, Chicago – USA
May 08 – 11, 2015
BST-CarGel®
A novel, minimally invasive, one-step cartilage regeneration system for all synovial joints

Defining the standard in clinical trial evidence in cartilage regeneration

Superior outcomes in tissue quantity and quality

The solution for sustainable and consistent high quality tissue
Past President’s Reflections

It’s been 6 months since I stepped down from the role of ICRS President and I have had time to reflect on the whirlwind of events I dealt with during that time. The early months of my term of office were dominated by the need to settle our legal dispute with Webstage that was threatening to wrap us up in expensive judicial processes for many months with no certainty about the outcome. The key to reaching a solution was to put aside our feelings on the case and deal with the reality that it would be cheaper and easier to reach a settlement early than to pay the price that comes with waiting for justice. I went to Zurich in September 2012 and together with Chris Erggelet attended a pre-trial hearing where the judge gave his views and pressed both sides very hard to settle. The judge was young but wise and did his job well. Chris had the important task of translating the discussions from German to English as we went along, as well as considering all options with me. In the end we found a way forward that cost some money in the short term, but has given us long-term financial stability. I am very proud of the work Chris and I did in that courtroom on behalf of ICRS members.

At the same time, the Executive Board and Industry liaison committee were working very hard to put in place longer-term agreements with our major sponsors to provide us with a more certain in-flow of finances during the periods between our World Congresses. It gave me great pleasure to see the ICRS Board members working so hard to secure these deals and we should all be grateful to Ken Zaslav, Jack Farr and Daniel Saris for leading this very important work.

The academic highlight for me was the ICRS Summit in Tallinn. Putting together the list of speakers and shaping the plan for the event with Mats Brittberg was enormous fun and it is fantastic that we had an almost 100% acceptance of the invitations to speak, which made life very easy. The event was very popular amongst members and so unfortunately we were not able to accept all applications to attend. The Summit itself involved a large amount of interesting discussion and debate by the audience. This is hard to achieve in larger conferences and was a key feature of the Summit style. We are still working on getting review articles written by the speakers for publication in “Cartilage” so that all members can share in some of the ideas that were topics for discussion.

Planning for the World Congress in September 2013 had been going on for some time and we were very keen to move to a new part of the world with Asia high on our list. Provisional plans for the meeting to be held in Japan were proving problematic because of the aftermath of the terrible earthquake and Tsunami in 2011 and uncertainty that came with it. In the end we opted for Turkey and finally settled on Izmir as the venue. Little did I know that this would itself prove to be a problematic choice because of the political unrest in Turkey that became very public as the year 2013 progressed. In June we were facing calls from various directions to cancel the event or move it to another location. I consulted with the mayor of Izmir, with the local scientists and clinicians, legal advisors and with our sponsors. We had an emergency meeting of the General Board where we unanimously decided that we should continue with the plans for Izmir. I believe that was the only decision we could make and it proved a good one as we had no problems from political activities, though attendance at the meeting was perhaps a little lower than it would otherwise have been. It was a stressful time for me as President and for Stephan Seiler and his excellent team in the ICRS office. But in the end we got through it and all was well.

My final legacy to ICRS from my term of office will, I hope, be an enhanced role for basic scientists in Society activities. At the Izmir meeting I announced that we will be running an ICRS Scientist Travelling Fellowship to parallel the clinical fellowship that has been running for some time. It will come into reality in the run-up to the next World Congress in Chicago. I hope that all young scientist members will consider applying for this fellowship and, if successful, taking part in what I hope will be a career-changing experience.

I leave the society in good hands with Chris Erggelet and I am now enjoying being in the back seat of the car rather than the driving seat – now it’s time for Chris to experience the ups and downs of a Presidential life.

Anthony Hollander, ICRS Past President 2012 - 2013
Welcome to Melanie Twerenbold our new Junior Executive Assistant

As you might already be aware, our office colleague Ms. Sandra Kessler has left the ICRS in December 2013 and she has now been replaced by our new colleague Ms. Melanie Twerenbold. Melanie holds a Bachelor of Science in Hospitality Management from the world famous Hotel Management School in Lausanne and has she already gained her first international working experiences in the hospitality industry in Sri Lanka as well as in Switzerland.

Born and raised in the tropical Island of Sri Lanka, she has learned to embrace a multitude of cultures and traditions whilst holding her Swiss heritage. Her mother tongue is English and Swiss German, while she is also competent in French and German and has some basic knowledge in Italian and Singhalese (National Language of Sri Lanka). Melanie likes practicing several sports like football, golf, and tennis as well as spending some spare time on the beach learning water sports. Melanie is also a huge fan of cats & dogs and has she volunteered and donated to several charities to help strays and support animal shelters.

Melanie is enthusiastic in having joined the ICRS and she is keen to act as our main office contact for any membership or registration issues but she will also support the office in many of the exciting upcoming projects.

Email: Melanie.twerenbold@cartilage.org,
Phone: +41 44 503 73 71

#DidYouKnow? – ICRS Web & Social Media Performance Unveiled

It has been more than a year since we have launched the new design of www.cartilage.org with integrated mobile site along with considerable digital marketing efforts and with a new social media presence on various networks such Facebook, Twitter, and Linkedin.

www.cartilage.org
10,000+ active users/month
a 150%+ increase

We are pleased to share with you some results: currently our website has reached close to 10,000 monthly users, which represent a 150% increase compared with the previous year. We have learnt a lot from the web and social data gathered. Over time, our ultimate goal is to be able offer a personalized and responsive web (coming soon) experience for our members, partners and public.
#DidYouKnow? – ICRS Web & Social Media Performance Unveiled

ICRS Facebook Page: Did you know that the ICRS Facebook page has now over 5,000 fans - twice as much as the AAOS or 10 times more than EFORT? Each post reaches an average number of 3,500 persons and we are still experimenting...

5,000+ fans

The ICRS Twitter Channel @CartilageRepair has gained 1000% increase in followers during the last 12 months. Did you know that one single tweet about the #HydroZONES project (by Jos Malda) has reached almost 100,000 people around the world?

A key challenge for the Executive Office is to distribute interesting, relevant updates as well as breaking news in the field of cartilage repair. As our executive team does not stem from a medical background, we take extra precaution when posting to our social media, as our strategy is to convey significant topics of everybody’s interest on cartilage repair. With our newly joined ICRS “Social Media Evangelists” Martin & David, we hope to leverage the growing ICRS LinkedIn Group further to steer scientific discussion and an increased community engagement.

To expand our reach to those interested and involved in Cartilage Repair, we have made ourselves available on different channels. The LinkedIn group conveys professional and provoking scientific discussions, while sharing relevant news from the ICRS family and the industry. Facebook, Twitter and Google+ channels deliver various news from the ICRS, the Executive Office, the industry, research, and interesting findings and of course, sometimes some fun as well.

Some future developments online, in which many are already in the pipeline are, the Public & Patient Platform, the ICRS responsive website (the content will automatically adapt to size of device screen used), the ICRS blog (if you are interested to be a blogger, please drop us an Email!) and more...
Social media networks play an important role in informing, educating and entertaining a community of people sharing the same interests. The ICRS is aware of the increasing importance of Facebook, LinkedIn, and Twitter, and therefore initiated a subgroup of the Communication & Publication Committee, of which Alan Getgood is the current chair.

Our new ICRS Online Community Managers/Social Media Evangelists will focus on maintaining and moderating relevant cartilage related content on our social media platforms. The new subgroup will start with two ICRS members. Two more will be added over the course of time. Martin Wiewiorski and David Stelzeneder, two junior ICRS members and former ICRS travelling fellows will rise to the challenge:

- Martin Wiewiorski is a junior consultant at the University of Basel Orthopedic department. His main area of interest is cartilage imaging and osteochondral repair of the ankle joint. Of many honors, he is a former Harvard University research fellow, EFAS and ICRS travelling fellow, and Swiss National Foundation scholarship holder.

- David Stelzeneder is a resident at the Medical University of Vienna/Vienna General Hospital in Austria. His research is focusing on magnetic resonance imaging of the knee, hip and spine and sports medicine. He is a former ICRS travelling fellow, and the current president of the Young Scientist Association at the Medical University of Vienna.

Martin and David are highly active in research, traveling and lecturing at conferences across the globe. Both are active Facebook, Twitter and LinkedIn users, having insight into and understanding the mechanisms and importance of the commonly used modern social media platforms. Their primary assignments will be to initiate and moderate scientific discussions and sharing cartilage repair related news and developments. Secondary goals will be to maintain a link between travelling ICRS members, and to arrange informal get-togethers (sports, nightlife, socializing) during conferences around the globe. They will look forward to taking on this new position and provide the ICRS community with exciting news and from the world of cartilage repair.

Please participate and contact Martin and/or David, if you have any questions or if you want to post something interesting on the ICRS Social Media Network.

Martin Wiewiorski: wiewiorskim@gmail.com
David Stelzeneder: david.stelzeneder@meduniwien.ac.at
The ICRS Social Media Evangelists
With the augmented number of ICRS educational activities, our office team is also challenged with increased marketing & travelling engagement to adequately fulfill our mission to promote our association and the many ICRS events in different parts of the world.

Early this year, we have already attended the AAOS in New Orleans, the Freiburg Cartilage Days in Germany, the Isokinetic Congress in Milan as well as the EFORT Congress in London. Furthermore, we have shipped ICRS promotional material to several other important cartilage events such as the Edinburgh Cartilage Symposium, ESSKA in Amsterdam, The TOBI in the USA, the UK Cartilage Club Meeting, the AFAS Cartilage Meeting on the Ankle in Prague, the Berliner Cartilage Symposium in Germany and many others.

The ICRS remains a small organization compared to all the other big players, with their sophisticated displays and modern equipment. However, our strategy is to create an impact through our warm hospitality and through our competent, friendly, engaging, professional staff. Generally, the interest in the ICRS is high everywhere and we always manage to recruit a few new members, as well as some new registrations for our upcoming educational events. Furthermore, many of our members stop by our stand when we then have some of those rare opportunities for short face-to-face chats with real people – something which unfortunately does not happen very often in our office in Zurich, where rather impersonal email communication predominates our professional life.

Further to these essential marketing activities, we are also confronted with many travels for site visits to gain adequate organizational information for our own planned educational events. Chicago, Larissa, Berlin, London, Gothenburg and Naples have already been visited this year as potential candidate cities for upcoming ICRS courses or congresses and many more to come.
Message to our Industry Partners

Cartilage & Meniscus Repair related Product Listing on the ICRS Website www.cartilage.org

The ICRS is currently working on a new Patient & Public Information Platform, which is planned to go online later this year with updated & accurate information on the field of cartilage repair and related technologies. To meet our objectives, we are now reaching out to our industry partners in order to gather input on what cartilage repair/regeneration products, techniques and procedures are available on the market. Our goal is to collect practical information and indications that will help healthcare professionals and patients to make informed decisions on cartilage-related disease or injury, and make them aware of the different treatment options.

We invite companies from around the globe, whose technologies can diagnose, evaluate, rehabilitate, repair, protect or regenerate cartilaginous surfaces of joints (stem cells, growth factors, PRP, bioactive composites, synthetics, scaffolds, allografts and combinations of thereof) to list their products on our site (even if the product is still in clinical trial phase only). If your company has more than one product/device, we kindly ask you to fill in one separate entry for each.

Cartilage & meniscus repair related technologies are divided in the following main categories: Diagnostics, Scoring & Evaluation Devices; Conservative Treatments such as Physiotherapy & Nutraceuticals; Growth Factors & PRP; Surgical Techniques; Cell Based Cartilage Repair; Biomaterials & Scaffolds; Implants/Resurfacing for Cartilage Repair; Drugs; Pharmaceutical & Laboratory Devices and others.

It will only take a few minutes to list your products! Access the Patient & Public Section on our website to list your products. Many companies already listed more than 50 products – add yours now!

Thank you very much in advance for your cooperation.

Report from Past ICRS Meetings

ICRS Focus Meeting – Stem Cells & Scaffolds hold on December 5-6, 2013 at the Istituto Ortopedico Rizzoli in Bologna, Italy

Course Directors: Maurilio Marcacci & Christoph Erggelet, Programme Chair: Elizaveta Kon; Scientific Committee: Giuseppe Filardo, Stefano Zaffagnini, Berardo Di Matteo, Francesco Perdisa

On December 5-6th 2013, one of the most historical and prestigious orthopaedic centres in Europe, the Rizzoli Orthopaedic Institute in Bologna, Italy, hosted the ICRS Focus Meeting concerning stem cells and scaffolds. Over 300 participants and 20 industry partners from 40 countries registered for this unique event, demonstrating the current great interest on this fascinating topic. The purpose of the congress was to summarize the current scientific and clinical evidence regarding the application of scaffolds and stem cells for joint tissue regeneration, bringing together the top experts in the field, from basic scientists to orthopaedic surgeons. The meeting started with a basic science perspective to give an overview of the state of the art and the need for stem cells applications; many aspects of mesenchymal stem cell (MSC) biology must be understood in regards to their action, to improve tissue engineering techniques and to increase the chances of successful tissue regeneration. Among the many challenges in this field, it is important to define a subset of markers able to predict MSC functional capacity.

Numerous scaffold options are available for cartilage defect repair, with or without cell addition, which are showing promising results, but high quality studies, with large groups of patients and mid to long-term follow-up are still lacking, in order to define the best indications. The hosting Rizzoli Orthopaedic Institute reported the experience on a biomimetic osteochondral scaffold, enriched by a live surgery demo performed by Maurilio Marcacci. The second meeting day addressed the subject of expanded and cultured MSCs, a popular topic for discussion in the application of stem cells. The clinical experience combining
bone marrow concentrate (BMC) and scaffolds showed overall good results both in ankle and knee joints, highlighting also the importance to identify the ideal patient that may benefit more from this kind of treatment.

In the field of meniscus regeneration, the BMC concentrate is also offering promising results with a simple but effective technique, as shown by the live surgery performed by Peter Verdonk and Stefano Zaffagnini, who combined a meniscal scaffold implantation with the administration of freshly harvested BMC. On the other hand, the use of cultured mesenchymal stem cells is also producing good tissue integration in the treatment of cartilage and meniscal pathologies, even though potential disadvantages might be linked to an extensive manipulation.

The honorary lecture by Arnold Caplan opened a new perspective in the stem cells approach, identifying them mainly as a potent multi-drug and site-specific delivery vehicle. This innovative concept postulates that MSCs don’t act just as stromal cells. Stroma is a generic term for connective tissue found in and around almost all organs and tissues. MSCs are found as perivascular cells and, in large vessels, in the adventitia, but not in the generic connective tissue. MSC function is of perivascular cells (pericytes) until a focal injury occurs. Then they are released at the site of injury and act as MSCs, providing molecular assistance in the activities related with tissue regeneration. The presence of more than 350 studies on the register of clinical trials confirms how these cells are raising interest among the research community.

Another interesting topic was the mini-battle for and against the use of allogeneic stem cells (Daniel Saris vs Frank Berry). The use of allogeneic cells might overcome the morbidity associated with the tissue harvesting and the lower proliferation and differentiation ability demonstrated by MSCs of OA subjects. However, while undifferentiated MSCs are well tolerated, differentiated cells are subject to immune recognition in immune-competent hosts. Thus, further studies are needed. The session on early clinical experiences showed that intra-articular injections are the most widespread option for MSC delivery, mainly due to the minimally invasive nature. However, there is no consensus about cell source. Promising results have been obtained with adipose-derived MSCs and BMC, but the umbilical cord blood and peripheral blood-derived MSCs are also emerging as valid options for the treatment of cartilage lesions.

When dealing with cartilage regeneration, paying attention to the joint environment is mandatory. When injury occurs, joint homeostasis is altered, and the therapeutic approach must take into account the restoration of a correct environment. In this scenario, numerous appealing treatments are available such as the use of growth factors (especially through platelet concentrates) or pulsed electromagnetic fields, which represent an appealing approach to favour the healing of and/or promote the engraftment and the proper development offered by various cartilage repair techniques.

The Venue of the Focus Meeting highlighted that numerous steps forward have been made concerning scaffolds and stem cells therapies, confirming that these fascinating biological approaches are close to be a tangible clinical option today. However, we should still improve our knowledge on MSC source and mechanism of action in order to translate these biological discoveries and early clinical experiences into effective and easily usable clinical protocols.

Elizaveta Kon, Programme Chair, Bologna, Italy
Report from 3rd UK ICRS Cartilage Club Meeting
5th – 6th April, 2014
Course Chairmen: Tim Briggs & James Richardson
Course Convenor: Anan Shetty
The third outing of the annual UK Cartilage Club meet- ing was a resounding success with more than a dozen international speakers. The talks covered all aspects of cartilage repair with an emphasis on established techniques and the advent of newer techniques. Imaging, rehabilitation and cartilage research were also discussed. The lunchtime workshop on latest cartilage repair techniques was well attended. The ICRS executive board was represented by Norimasa Nakamura.

The ESSKA Springer book Techniques in Cartilage Repair Surgery edited by Shetty, Kim, Nakamura and Brittberg was unveiled by Prof Mahadevan of the Royal College of Surgeons of England. Mats Brittberg was honoured with the Lifetime Achievement Award and Prof Umezawa was presented with the Scientist Award by SK Research Foundation and Canterbury Christ Church University.

The venue for the meeting was the historic Chatham Maritime campus of the Canterbury Christ Church University in Kent, UK. Fortunately, the weather was excellent and the attendees could enjoy the British spring. The conference dinner was held at the scenic Gillingham Golf Club and was well attended. Additionally, the meeting was accredited by the Royal College of Surgeons of England for 9 points.

Report from the UK Cartilage Consensus Meeting & Edinburgh Cartilage Symposium
On 23rd March 2014, UK cartilage repair surgeons and rehabilitation specialists met in the historic Royal College of Surgeons of Edinburgh. The aim was to discuss the status of cartilage repair surgery in the UK, and produce an evidence-based consensus document regarding the optimal first line and salvage surgery for isolated articular cartilage lesions of the young adult knee. The clinicians presented acknowledged the value of such a position statement in response to the complex interaction of health service funders, industry, regulatory bodies and licensing authorities that have rendered some surgeons unable to provide the evidence-based best available treatment for their patients. The meeting was expertly refereed by a non-medical chairman in the absence of any industry representation, and delegates had full access to the cartilage repair literature. The meeting was inclusive and productive. The consensus paper will follow, and will be circulated in draft to all those present, all members of the ICRS in the UK and all members of the British Association for Surgery of the Knee for their contributions before publication.

On 24th March 2014 the first Edinburgh Cartilage Symposium was held. International faculty included Professors Brittberg, Saris, Richardson, and Shetty. Local surgeons and scientists made valuable contributions. The educational symposium was aimed at surgeons who see patients with articular cartilage lesions but may not necessarily have a specialist practice in this field. The basic science, indications, techniques, outcome, rehabilitation and case studies were discussed. A cadaver workshop followed, where delegates were shown arthroscopic and open techniques commonly used to treat cartilage defects in the knee and ankle, and were able to perform these under expert guidance on the cadaver specimens. Tips and tricks were freely exchanged. We are grateful to our Industry partners for their support of this event. We look forward to welcoming colleagues to Edinburgh for the next meeting on 16th March 2015.

Leela C Biant, Edinburgh, UK
My experience with the ICRS/Zimmer scholarship can be simply summed up as incredibly educational. As a new member to ICRS as well as a junior academic surgeon with an interest in building a cartilage regenerative practice, the traveling fellowship offered me an opportunity to learn from the international community in both basic science and clinical applications.

I started my journey in Antwerp, where my hosts were Peter Verdonk and Koen Lagae. For the week, the sheer volume of cases in Verdonk’s and Lagae’s knee practice was as impressive as the necessary efficiencies. With each operative case, they pointed out small but significant pearls that I have already applied to my own surgical technique. Although no meniscal implant/transplant or cartilage cases were observed, there was a large variety of cases that spanned from sports to reconstructive cases. I gleaned an understanding of treatment algorithms and intra-operative decision making for potential complications from a different point of view, as compared to how I tackle these issues. In addition, I was able to observe and perform the monoloop reconstruction technique in conjunction with ACL reconstruction. In between cases, Peter Verdonk shared some of his current research, which may open doors for international collaboration. On my off time, which was mainly on the weekend, Antwerp was charming and easy to navigate. During my weekend touristic trek through Ghent and Bruges, I wondered how Belgians could remain so thin compared to Americans as I subsisted on waffles, chocolate, and beer.

The next stop on the agenda was University Medical Center Utrecht, academic home of Daniel Saris and his co-hosts, Jos Malda and Tommy de Windt. My visit started with an inpatient OR day, where amongst the cases were two ACI procedures and a revision ACL with meniscal substitute implant were performed. Daniel Saris introduced me to surgical techniques and an instrument set that “revolutionized” how I looked at surgical management for cell therapy for osteochondral lesions. We performed a “sandwich” procedure for a condylar osteochondritis dissecans lesion, something I had been planning on one of my own patients, but had never before performed. I have since implanted that patient who is doing well.

Utrecht demonstrated a unique integration of basic and clinical science that results in a successful translational science medical center. They were in the midst of recruiting patients for preliminary safety studies for a one-step cell-based therapy utilizing banked stem cells in addition to the patient’s own isolated “chondrons.” In the clinic, I observed follow-up for patients undergoing joint distraction for treatment of severe osteoarthritis and was able to discuss the technical aspects with the rheumatology and orthopaedics lab. Understanding and observing their approach and synergy in the management of logistics for a large referral center that manifested itself as seamless patient care was also educational and directly applicable to working at my university. On a personal note, one of the highlights of the week was to sit down and have a pizza dinner with Daniel Saris and his sons at his lovely home.

The Equine clinic was equally as impressive, boasting a facility that can house well over 100 horses at a time. During my tour, a group of veterinary professors and students were working up a horse for a lame gait in a teaching rounds format. I was very much impressed with the clinical acumen of the veterinarians and noted the similarities in the care of our own more verbal patients. The week was concluded with an outpatient operative day, coming full circle in cartilage techniques with a microfracture procedure.

The final leg of my journey brought me to the renowned Rizzoli Institute in Bologna, Italy, where I was graciously hosted by Elizaveta Kon and Giuseppe Filardo. The city’s rich history and architecture complemented the experience of my tour. My time was spent observing the operating theater with Maurilio Marzoccchi’s team and the research laboratory facilities. Among the cases observed involving meniscal deficiencies, I was able to observe engineered meniscal scaffold implantation, something I had not seen in the US. In addition to the many firsts, this was also the first time I observed MaioRegen implantation for an osteochondritis dissecans lesion. The week was topped by a dinner at Elizaveta Kon’s home, where I sampled genuine Bologna cuisine.

I had applied for the fellowship with the goal of gaining technical expertise from cartilage centres and also gaining exposure to innovative technologies. The Zimmer traveling fellowship allowed me to far exceed by initial goals. The international exchange gave me technical pearls and perspectives I had not consciously considered. As a result, I feel I have become a better and more insightful clinician and researcher. I am grateful for the opportunity that has already influenced me tremendously across multiple facets of my practice, and I am sure will continue to influence me in the years to come.

Cassandra A. Lee, MD, Assistant Professor UC Davis Health System, Dept. of Orthopaedics, Sacramento, CA - USA
Event Calendar

2014
06.06 - 07.06, 2014
5th Annual PRP & Regenerative Medicine Symposium with Cadaver Lab
Las Vegas, US
www.prpseminar.com

03.07 - 04.07, 2014
ICRS Focus Meeting - The Knee
International Cartilage Repair Society
Zurich, CH
www.cartilage.org

11.09 - 13.09, 2014
33rd EBJS 2014
European Bone & Joint Infection Society
Utrecht, NL
www.ebjs2014.org

18.09 - 20.09, 2014
AGA-Congress 2014
Innsbruck, AT
www.aga-kongress.info

23.09 - 27.09, 2014
12th TUSYAD Congress
Izmir, TR
www.tusyad2014.org

23.10 - 25.10, 2014
5th ICRS Surgical Skills Course (Wet -Lab)
International Cartilage Repair Society
Larissa, GR
www.cartilage.org

27.10 - 30.10, 2014
5th ICRS Laboratory Skills Course
International Cartilage Repair Society
Fort Collins, CH
www.cartilage.org

2015
14.01 - 17.01, 2015
2nd ICRS Summit
International Cartilage Repair Society
Zermatt, CH
www.cartilage.org

26.02 - 27.02, 2015
ICRS Focus Meeting - Allografts
International Cartilage Repair Society
Brussels, CH
www.cartilage.org

24.03 – 28.03, 2015
AAOS 2015
Las Vegas, USA
www.aaos.org

28.03 – 31.03, 2015
ORS 2015
Las Vegas, USA
www.ors.org

30.04 – 03.05, 2015
OARSI 2015
Washington, USA
www.oarsi.org

07.05 – 08.05, 2015
6th ICRS Surgical Skills Course
International Cartilage Repair Society
Chicago - Rosemont, US
www.cartilage.org

08.05 - 11.05, 2015
ICRS 2015 - 12th World Congress
International Cartilage Repair Society
Chicago, US
www.cartilage.org

27.05 – 30.05, 2015
EFORT – Congress 2015
Prague, CZ
www.efort.org

07.06 – 11.06, 2015
ISAKOS 2015
Lyon, France
www.isakos.com

17.09 - 19.09, 2015
AGA-Congress 2015
Dresden, DE
www.aga-kongress.info

15.09 - 17.09, 2016
AGA-Congress 2016
Basel, CH
www.aga-kongress.info

This listing is not complete and does not constitute a recommendation or endorsement by ICRS. Further investigation by interested parties is always necessary. For further information, visit the ICRS online event calendar at our website.
Upcoming ICRS Educational Events

5th ICRS Surgical Skills Course (Hands-on Wet-Lab)
October 23 – 25, 2014, University of Thessaly, Larissa – Greece, “Cartilage Repair – Understand it, see it, do it”

Internationally acknowledged surgeons and experts in the field of cartilage repair will provide you with the newest information, tips and tricks of all options in the surgical treatment of chondral lesions. This outstanding academic programme includes scientific lectures, live demonstrations, and hands-on workshops on human cadaver specimens. The course will include core lecture modules for cartilage and osteochondral repair. Each module will handle a specific area (cartilage repair techniques, meniscal repair and replacement, patellofemoral joint problems management, osteotomies) in order that the delegate will acquire knowledge on the field of his/her training.

Course Highlights: 4 x 1.5 hours Hands-On Human Cadaver Workshops; Bio-Surgical Solutions; Cartilage Repair Techniques; ACL, Meniscus, Osteotomies, Microfracture; Stem Cells & Tissue Engineering for Cartilage Lesions; Basic Science in Cartilage Repair; Cartilage in Osteoarthritis

Early Bird Registration Deadline: June 30, 2014.
For further information on programme, faculty and registration, please visit our website.

5th Laboratory Skills Course for Translational Science
Hands-on Course & Lectures “From the Lab to the Clinic”, Colorado State University, Fort Collins, Colorado, USA, October 27 – 29, 2014

Who should attend? Research Scientists in academics and industry, clinicians, residents, graduate students, post-doctoral fellows who have interest in expanding their laboratory skills in advanced techniques for cartilage repair and in learning about how to translate laboratory findings through clinical testing and analysis for cartilage repair. The ICRS laboratory skills course will be held at Colorado State University in Fort Collins, Colorado, USA in October 2014 for all those interested in improving their knowledge and skills in techniques commonly used in cartilage resurfacing animal models, preparing cell-based therapies from bone marrow and blood, and clinical imaging.

Hot Topics: This three-day workshop will encompass techniques to evaluate regenerative medicine techniques in live animal cartilage repair models. Each module will consist of morning lectures by experts in the field, followed in the afternoon by hands-on laboratories. The first module will focus on techniques for creating critical-size cartilage defects. The second module will focus on cells and scaffolds, with an emphasis on techniques for preparing blood and bone marrow for platelet-rich plasma and mesenchymal stem cells, respectively. This module will also include clinical techniques for implanting hydrogels into cartilage defects. The third module will focus on imaging techniques for analysing repair cartilage formation at the end of live animal studies. Participants will not only have the opportunity to hear lectures, but more importantly, to have a chance to partake in the practical, hands-on experience in a range of techniques presented in the lectures.

This course is chaired by Wayne McIlwright and John Kisiday. For further information on programme, faculty and registration, please visit our website.

2nd ICRS Summit “The Aging Cartilage”
Zermatt, Switzerland from January 14 – 16, 2015
Organised by Chris Erggelet & Anthony Hollander

Style of the meeting: The idea of a Summit is based on the well-established “Gordon” and “Keystone” conferences that bring together a select group of experts to discuss key scientific topics/themes. The Summit will include a small invited Faculty and 50 delegates, ideally including 15 basic scientists, 15 clinical scientists, 15 industry experts and 5 graduate students/trainees (at subsidised cost). We expect that there will be more applicants than places available in each category and therefore those wishing to become delegates will most likely need to compete for the available places. This will be through submission of a short statement about their contribution to the field of Cartilage Repair and to ICRS.
Upcoming ICRS Educational Events

Meeting format: The Summit will include a mixture of traditional lectures, extended discussion and debates on provocative themes. Each day will end with a wrap-up session where delegates and Faculty will together explore the ideas that have emerged. The intention is to stretch the limits of our thinking and challenge our preconceptions.

Scientific content: The Summit will look to new and challenging horizons rather than reviewing the current state of the art. The intention is to reach a consensus on what scientific, clinical and industrial work will need to be done if we are to make advances in providing new therapies for the treatment of cartilage lesions in older patients. Full details of speakers and timings are shown below.

Dissemination: In order that all ICRS members and a wider audience can benefit from the Summit, all faculty members will be required to write a review paper summarising their contribution. These reviews will be published in the ICRS journal, “Cartilage”.

Why you should attend: We intend this to be an exciting and forward thinking meeting that will allow everyone to collectively think "outside the box". You will hear about exciting science, clinical challenges and industrial reality and use this knowledge to explore challenging ideas about the whole joint and the whole patient.

 Venue: The Summit will take place at the historical Seiler’s Hotel Mont Cervin, Zermatt’s first hotel, built in 1852 and taken over by the Swiss hotel pioneer Alexander Seiler in 1857. Alexander’s son, Dr. Hermann Seiler, (Stephen Seiler’s Grandfather) organized Switzerland’s first Ski course here on January 12, 1902 and founded Zermatt as one of the worldwide first winter sports destination by opening his family-owned hotel property to an initial group of 180 British alpine winter tourists in 1928. Besides the famous Matterhorn, being the most photographed mountain in the world, Zermatt is surrounded by 37 other 4,000-metre peaks – almost half of all those existing in the Alps. Since the first ascent in 1865 by British Edward Whymper, who already was a guest at Seiler’s Hotel, mountaineers from around the world have taken on the challenge to reach the summit of the Matterhorn. It is estimated that over 500 alpinists have died on the Matterhorn since the first climb in 1865, making it one of the deadliest peaks in the Alps.

The registration fee includes accommodation and all food/refreshments. Further information on the application process, registration fees and scientific programme will be available on our website soon.

ICRS Focus Meeting – Allografts
February 27 – 28, 2014, Brussels – Belgium

The use of allograft tissue in Orthopaedic surgery has a long history spanning over 20 years. Currently, more than 1 million units of allograft tissue are used in the US per year, the majority in the form of bone grafts for procedures such as spinal fusion, fracture fixation and osteotomies. Approximately half of all ACL reconstructions in the US are performed with the use of allografts, including tibialis, achilles and patellar tendons.

Lastly, but of critical interest to our society, fresh osteochondral and fresh frozen meniscal allografts are used to reconstruct articular damage in more than 4000 patients per year. Whereas allograft tissue is readily available in the US, access remains limited in many parts of the world. The use of allograft tissue decreases donor site morbidity, and allows the management of conditions that otherwise have no treatment alternatives, such as the completely meniscectomized knee.

While not without limitations, allografts have improved the lives of countless patients worldwide. Its use, however, remains limited by supply, and political and regulatory issues. The ICRS hereby announces a meeting dedicated to finding solutions to these very limitations. It will bring together leaders from regulatory agencies, industry and physicians to create a forum for the exchange of ideas, discuss regulatory hurdles, and strategies to educate the public and health care providers about this exciting initiative. Stay tuned!

This course is chaired by Andreas Gomoll & Peter Verdonk. More information on the programme, faculty and registration will be available on our website very soon.
We would like to invite you to attend the 12th World Congress of the International Cartilage Repair Society. Set your sights on being in Chicago May 8-11, 2015 for this special event. The programme chairs and local organizing committee have planned a meeting that will be both provocative and entertaining. The setting will be on the shores of Lake Michigan and it will be springtime in the windy city. We are excited about providing a program that will be of interest to both clinicians and basic scientists with several new session topics and timely debates on clinical management. Several new sessions that cover emerging trends in our field will be spotlighted.

The clinical topics will include a comprehensive update on most of the available clinical strategies currently being performed. Current topics that are controversial will be hotly debated in special sessions. Additional new topics include spine [disc] and foot & ankle cartilage resurfacing, and many others. Basic science sessions will include a focus on topics such as bioprinting, biology of cartilage development, and biological and engineering considerations for optimal design of cartilage repair. In addition, sessions on controlled release and novel scaffold material for tissue engineering of cartilage are planned.

This congress will allow a continuation of our society’s goal in bringing together clinicians and scientists from around the globe to advance our knowledge of cartilage. It will be an excellent opportunity to enjoy a comprehensive overview of the state of the art in our field whether you are a clinician or scientist. The local organizing committee is poised to give you a taste of all the second city has to offer in addition to the Chicago style deep dish pizza! So please mark your calendars for joining us the next ICRS World Congress and we look forward to seeing you there!

Daniel Grande & Tim Spalding
Scientific Programme Co-Chairs

Brian Cole & Susan Chubinskaya
Congress Co-Chairs

Abstract Submission will be accepted from August 30 – November 10, 2014

ICRS invites you to submit your abstracts to the 12th ICRS World Congress, where professionals from around the world gather, to share the latest developments in cartilage repair.

Overall, our scientific programme is expansive in scope and deep in content in order to benefit scientists, clinicians and industry participants. If you wish to share your current research or present a new technology at ICRS 2015, you may do so by submitting your abstract for review until November 10, 2014! Our ultimate goal is to improve treatments for the patient, and the path towards this goal is through our unique combination of scientists, clinicians, and industry partners that only ICRS provides.

Congress Content: 4 Meeting Days with CME Accreditation; 100 Invited Speakers & Key Note Lectures; 7 Plenary Sessions; 23 Special Sessions; 150 Free Papers; 250 Posters; 9 Instructional Courses; 8 Industry Symposia; Panel Discussions & Debates; Technical Industry Exhibits. Congress Awards, Social Events & Spouse Programme.

Abstract Categories: Cartilage Repair in the Knee, Shoulder, Spine Foot & Ankle, Biomarkers, Proteomics & Genomics, Stem Cells, Chondrocytes, PRP, Growth Factors, Rehabilitation & Outcome, Biomaterials, Biomechanics, Scaffolds, Meniscus & Instability, Other Musculoskeletal Tissues, Osteoarthritis, Differentiation Media, Imaging, Small & Large Animal Models and others...

The ICRS programme committee encourages you to submit all work related to cartilage repair; if it does not fit into one of the proposed abstract categories – just tick the “other” box and we will appropriately review your work.

The preliminary programme and general information for the ICRS 2015 is already available on our website.

Mark Your Agenda:

ICRS 2015 World Congress, Chicago, USA

Surgical Skills Pre-Course: May 07 – 08, 2015
Congress Dates: May 08 – 11, 2015
Abstract Submission: Aug. 30 – Nov. 10, 2014
Early Bird Registration Deadline: May 15, 2015
ICRS is proud to announce a surgical skills course (wet lab) directly preceding the 2015 ICRS World Congress in Chicago. The course will be held on May 7 – 8 until noon at the brand new AAOS Orthopaedic Learning Center in Rosemont conveniently located close to Chicago’s International O’Hare Airport. The 6th ICRS Surgical Skills Course will encompass a review of the international perspective on cartilage repair, meniscus management and associated procedures related to the comprehensive management of the young arthritic knee. Participants will enjoy a balance of didactic lectures, case presentations and a hands-on cadaveric (arthroscopic & open surgery) experience.

At the end of this 1.5 day course, participants will be shuttled to the downtown Chicago Sheraton for the ICRS World Congress to continue this unique experience. Participants will be required to book their accommodation for the pre-course at our official Hotel in Rosemont from May 6 – 8, 2015. A separate registration fee for the skills course is required as this workshop is not included in the regular world congress registration fees. For further information, accommodations, programme and faculty, please visit our website.

Why Chicago?
Affixed by the stunning Lake Michigan and decorated with inspiring architecture, Chicago is more than just a big city. Besides its striking downtown area, which includes some of the tallest buildings in the world, Chicago has a distinctive coastline, hundreds of vibrant parks and more than 200 unique neighbourhoods. It’s this truly distinctive mix of incredible attractions and cultural allure that make Chicago one of the friendliest, most liveable cities in America.

Chicago’s developed a reputation as a must-visit destination for diners. In fact, Chicago is one of only three cities in the country to have its culinary chops rated by the prestigious Michelin Guide. With incredible shopping on The Magnificent Mile, world premiere performances in its famed Theater District and one of the country’s most active nightlife scenes, this city is always buzzing. Chicago also vaunts more than 40 museums, five regional Tony Award-winning theatres and, no matter the season, there’s always a professional sports team to cheer to victory.

Situated squarely in the center of the country and equipped with two major, international airports, getting to Chicago is easy. Once you arrive, you’ll be able to choose from more than 30,000 hotel rooms in the downtown area alone. From sleek downtown properties to luxury boutiques, you will discover outstanding accommodations for every style and budget.

Millennium Park, deep dish pizza and Wrigley Field are all compelling enough reasons to visit Chicago, but the city’s most endearing quality is its people. Chicago’s neighbourhoods represent more than 100 countries and it’s through this diversity and profound city culture that we are able to develop the country’s best restaurants, theatres and museums. Enjoy your visit to Chicago. We hope to see you again soon.
Basic science study – Dennis Evseenko, University of California Los Angeles, USA

Review on: ‘Cartilage-specific deletion of Mig-6 results in osteoarthritis-like disorder with excessive articular chondrocyte proliferation’

Ben Staal, Bart O. Williams, Frank Beier, George F. Vande Woude, and Yu-Wen Zhang.

Mitogen-inducible gene 6 (Mig-6) is important for maintenance of joint homeostasis. Genetic ablation of Mig-6 in mice results in a phenotype similar to osteoarthritis (OA) in multiple synovial joints. However, it was unclear in which cell type Mig-6 was expressed and what cells were causal for developing the OA-like phenotype. In a paper recently published in PNAS, authors reported that Mig-6 is uniquely expressed in the cells surrounding the entire surface of the synovial joint, including chondrocytes in the superficial zone of the articular cartilage and in the meniscus, and synovial lining cells. Their data showed that chondrocytes play a critical role in developing the OA-like disorder in the knee. However, other cells are likely required for full development of the Mig-6–deficient joint phenotype.

In the paper, a Mig-6/lacZ reporter mouse strain expressing β-galactosidase under the control of the Mig-6 gene promoter was generated to determine Mig-6 expression in joint tissues. By β-galactosidase staining, authors showed that Mig-6 was universally expressed in the cells across the entire surface of the synovial joint, including chondrocytes in the superficial zone of articular cartilage and in the meniscus, as well as synovial lining cells. By crossing Mig-6–floxed mice to Col2a1-Cre transgenic mice, authors generated cartilage-specific deletion of Mig-6. Their data demonstrated that deficiency of Mig-6 in the chondrocytes results in a joint phenotype that only partially recapitulates the OA-like disorder of the Mig-6–deficient mice. This means ubiquitous deletion of Mig-6 led to the OA-like disorder in multiple joints, whereas cartilage-specific deletion affected the knee joint only. Furthermore, chondrocytes with Mig-6 deficiency showed excessive proliferation along with enhanced EGF receptor signaling in the articular cartilage and in the abnormally formed osteophytes. This paper provides insight into the crucial role played by Mig-6 in maintaining joint homeostasis and in regulating chondrocyte activities in the synovial joints.

Clinical Study-Michael I. Iosifidis, Thessaloniki, Greece

Review on: ‘Intra-Articular Injection of Adult Human Mesenchymal Stem Cells: a safe procedure that offers to tissue regeneration’

C. Thomas Vangsness Jr., MD, Jack Farr II, MD, Joel Boyd, MD, David T. Dellaero, MD, C. Randal Mills, PhD, and Michelle LeRoux-Williams, PhD


In recent years mesenchymal stem cell (MSC) treatment strategies have emerged as a powerful tool for tissue repair and/or regeneration, thanks to their ability to differentiate into a variety of connective tissues. The regenerative effects of MSCs are due to their structural contribution to tissue repair and their immunomodulatory and anti-inflammatory action, through direct cell-to-cell interaction or secretion of bioactive factors. MSCs have a capacity for self-renewal, stemness maintenance and can migrate toward injured tissues (homing/trafficking) where they display reparative effects (plasticity).

However, knowledge about these strategies is still preliminary, as demonstrated by the prevalence of preclinical studies, whilst clinical studies are of low scientific level due to questionable methodology, small numbers of patients, and short-term follow-up. Nevertheless, the available studies suggest a potential for these cell-based treatments to be developed in many directions. Many different cell sources are available and there is the potential to use them concentrated or after in vitro culture. They may be delivered to the site via simple injection, or surgically, alone or augmented with growth factors or scaffolds, and many other improvements are being developed and subsequently studied. Studies using allogeneic MSCs are also appearing, as there is a great interest for studies that overcome all the above-mentioned limitations, drawbacks and concerns.

This study under review tried to overcome these by performing a randomized, double-blind, controlled study (therapeutic Level I) to investigate the safety of the intra-articular injection of human allogeneic MSCs into the knee, the ability of MSCs to promote meniscus regeneration following partial meniscectomy, and the effects of MSCs on osteoarthritic changes in the knee.

Fifty-five patients from seven institutions underwent a partial medial meniscectomy, and after seven to ten days a single superolateral knee injection was given. Patients were randomized to three treatment groups: Group A received an injection of 50×10⁶ allogeneic MSCs; group B, 150×10⁶ allogeneic MSCs; and the con-
trol group, a sodium hyaluronate injection (hyaluronic acid/hyaluronan). Patients were followed to evaluate safety, meniscus regeneration, the overall condition of the knee joint, and clinical outcomes at intervals through two years, and the evaluation also included sequen- tial MRI.

The results demonstrated that high doses of allogeneic MSCs can be safely delivered in a concentrated manner to the knee joint without abnormal tissue formation, and without adverse events that led to treatment discontinuation or study termination. It is important to mention that sequential immunologic, hematologic, and urine testing showed no clinically significant trends.

The clinical outcome for pain reduction was encouraging comparing with the controls in one and two years points, which is more important due to double-blinded study design. However, the Lysholm clinical score failed to show a similar effect between the three treatment groups. There was significantly increased meniscal volume (defined a priori as a 15% threshold) determined by quantitative MRI in 24% of patients in Group A, 6% in Group B and no one in Group C. Nonetheless, it is quite challenging to quantify the meniscal volume through an MRI investigation.

Overall, this well designed study improves our knowledge about the safety and effectiveness of using allogeneic MSCs for intra-articular injections into the knee in humans.

Of course many aspects have to be optimized among all of these studies to support the potential of this biological approach, mostly for cartilage treatment and to compare advantages and disadvantages with the available treatments.

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**Interview with Robin Poole PhD, DSc.**

*Interview held by Al Getgood, London, Ontario, Canada*

“*It has been my pleasure to pose questions to Robin Poole regarding aspects of his life and work. I am sure you will find the responses are enlightening and provide a wonderfully honest insight into the mind of a great researcher*”

Robin Poole is Professor Emeritus of McGill University, Montreal Canada and recipient of the ICRS Lifetime achievement award, presented at the ICRS World Congress in Izmir in 2013. Following a career first as a microbiologist and then a cancer researcher, he started his research on arthritis at the Strangeways Research Laboratory and Department of Pathology, University of Cambridge (UK) working on cartilage degradation and joint inflammation. This led to an invitation to start a new Joint Diseases Laboratory at the Shriner’s Hospitals for Children, Montreal, and a paediatric teaching hospital of McGill University. He was made Professor, Department of Surgery at McGill University in 1981. His research has focused particularly in the areas of cartilage resorption in skeletal development and arthritis; immunity to cartilage antigens in arthritis; and the development of biomarkers to detect arthritic diseases, their progression and treatment. He has authored over 200 peer reviewed papers and published 90 reviews and trained over 40 graduate students and fellows. He has received a number of awards in recognition of his achievements. These include a Doctor of Science degree (Reading University); Kappa Delta Award for Excellence in Research (American Academy of Orthopaedic Surgeons); The Holley Award, (American College of Rheumatology), the Carol Nachmann Prize in Rheumatology for arthritis research and the Presidencies of the Canadian Orthopaedic Research Society and the 6th World Congress of Inflammation Research Associations. He was a founding member of the Canadian Arthritis Network, a National Center of Excellence, of which he is currently Scientific Co - Director. Robin Poole continues to participate in editorial, conference program and advisory boards, research and assessment review committees, both nationally and internationally. He is a Consulting Editor for the Journal of Clinical Investigation. He has been happily married for 40 years and has three grown children.

**AG: How did you decide that you wanted to pursue a career in medical research?**

RP: Way back in 1946 when I was 7 years old my father was diagnosed with cancer involving the lumbar spine. He was in agony most of the time. By chance, a Swedish clinician scientist working at the Westminster Hospital in London, England was developing what was then a possible new way of treating patients with cancer. It involved progressively destroying tumours with gamma radiation. It hadn’t been tried before and he was looking for volunteers. He told my father that he would probably die within 6 months but he might be able to cure him over a two year period with regular radiation sessions. He had nothing to lose. My father was cured and died of smoking-related causes when he was 70. This experience, hearing from my father of the steady progress made as the tumour was destroyed, bit by bit, left an enormous impression on me: somebody could cure my father and give him his life back again.

Again, about this same time, the family cat became very sick. She had an infection, trying to keep herself cool on the
Interview with Robin Poole PhD, DSc.

kitchen tiles. My mother and I nursed her back to health with brandy and milk from a fountain pen ink holder. I thought that she might have contracted an infection from the open outside drain where she was known to drink. I wondered what it was in that drain that might have caused the infection. Later, when I was eight, my father bought me a simple microscope so that I could examine the water. I was fascinated to find all these bacteria bobbing around, some of which might have made her sick. When I was about 10 the goldfish in my fish tank by my bed started to be covered in fungal growths: some died. I decided to treat them with a homemade concoction and the rest survived as the fungus disappeared.

So I guess becoming a scientist was in my blood and working on human diseases was my ambition. I went to Reading University in 1958 and studied microbiology combined with chemistry and zoology. After working with bacterial and viral pathogens in industry and being unable to publish any of my very original findings I realized that I must work in a more academic environment. I had this great urge to publish and share my findings with others. I found another job in cancer research. I had to switch fields as my ladylove, and now my wife of 50 years, was in London and I was unable to find a job in the London area in microbiology.

AG: Who were your mentors in your early career and why?
RP: Key mentors were Jack Lucy, Professor of Biochemistry at the Royal Free Hospital Medical School, University of London with whom I worked on membrane fusion (1968-70) after completing an external PhD at Reading. Jack introduced me to a more focused approach to science. The other major mentors from 1970-77 were John Dingle, who was to become Director of the Strangeways Research Laboratory in Cambridge, England and Alan Barrett, then a senior scientist in the same lab. John was a very inspiring person and Alan was an outstanding biochemist who taught me about proteases and how best to characterize them. Dame Honor Fell, previously the Strangeways director from 1928-1970, was the other great influence. Her experimental approach was based on organ culture, in which she was the pioneer. Dingle and Fell showed me vision and how much fun good science could be, and Barrett showed me the precision and importance of good methodology and experimental design. They all made me think deeply and maintain my focus on the research in hand. Dingle and Barrett had created a very critical environment, full of visiting scientists, mainly from the states, such as the always impressive Zena Werb, a Canadian fresh from her PhD at the Rockefeller University in New York City. It was Dingle who recommended me for the job in Montreal at the Joint Diseases Laboratory at the Shriners Hospital, McGill University.

AG: Your early career started in Cambridge, UK. Can you please describe your work at that time and how this led to you moving to Canada?
RP: In 1969 I was invited spend a week with Alan Barrett at the Strangeways helping him prove that the conclusions of a Nature publication on proteinases and arthritis were incorrect. After a week’s work we put our results together and published a paper in Nature that described our findings. Everybody, including Fell, was amazed that so much could be achieved in such a short time. Admittedly in that week I had worn out a pair of my only casual shoes, walking all over the rambling building, from cryostat to lab to microscope to dark room. But the stimulation of being with this world-leading group at that time, was incredible.

Subsequently, I was invited to join the group in Cambridge as their cytochemist with a mandate to develop new immunological methods to detect and observe proteases, both within cells and in extracellular sites in hyaline cartilages. I was working under Barrett’s and Dingle’s supervision, on proteolytic mechanisms involved in the degradation of cartilage matrix in development and arthritis using both chick embryo and human articular cartilage organ culture systems pioneered by Fell. Antibodies had been developed to lysosomal proteases that were suspected of causing cartilage degradation. I developed new antibody-capture ways of demonstrating the presence of extracellular proteases in living tissues using both cultured chick embryos, stimulated with retinol to resorb their extracellular hyaline matrix and cultured human articular cartilage and attached synovium from traumatized and rheumatoid joints. I also worked with Fell on the cellular mechanism of cartilage erosion in culture by soft tissues, such as by unstimulated synovium that was created by pig synovium and bone marrow stimulated with complement-sufficient serum. This work led to the identification by Jeremy Saklatvala of catabolin, also known as interleukin-1. Fell had predicted the existence of this molecule in the early 1970s just after her retirement from the Strangeways.

It was John Dingle who recommended me for the job in Montreal at the Shriners Hospital, and McGill University following an approach by Dick Cruess, then Chair of Orthopaedics at McGill and Chief Surgeon at the Shriners Hospital. Later Dick became Dean of Medicine for three terms. He generously invited me to design the lab and the Shriners built it for me, starting in 1976. I finally arrived in early March 1977. It was an amazing opportunity for a young scientist and one I could hardly refuse. But it was very difficult leaving behind families, friends, colleagues and many relatives. In the early 1970s, Dingle offered me the opportunity to present at a Gordon Conference on the macrophage, on his behalf, some of our work on inhibition of intracellular degradation of haemoglobin in macrophages by an antibody to the lysosomal protease cathepsin D. It was a terrific experience going to the USA for the first time, meeting so many eminent scientists and having the work so well received. I was invited to visit a number of labs and made many contacts for the future.

So every year after that I visited the states giving a talk on our work at various labs across the southern and eastern seaboard. With the $100 honorarium and free or subsidized accommodation I was able to self-finance my annual US visit. So when I moved to Canada I already had many colleagues in the USA with whom I had close contact.

AG: Having now worked in two countries, are there any lessons that either country could learn from each other, in terms of research infrastructure and funding (or other)?
RP: Research opportunities and jobs were very limited in
Britain when I was there. That is the main reason I left. Coming to Canada I had the USA at my doorstep, where almost all the research in my field was happening outside my old lab in Cambridge. In fact, my colleagues in Cambridge wondered why I was going to Canada. In their short-sited manner some said “there’s nothing there “referring, of course, to the research in my area of the basic sciences. But for me it was a great challenge and opportunity. Starting the lab from nothing was certainly something that attracted me. I knew nobody there and so had to advertise positions at the post-doc and technical levels. Peter Roughley joined me later in the year as a scientist and Brian Champion came over from Britain as my first graduate student. Ordering equipment, chemicals and other resources all took time as the companies were usually new to me. But I received excellent start-up funding from Shriners Hospitals and support from Dick Crueiss that made it a lot easier than in Britain. The job offered very many more opportunities. But it took two years to get most things sorted and the science on its way.

What I missed for years was a lack of similar interests and research in my area of basic research in Canada. But across the border, there were all sorts of groups with which I shared common interests. I sat on NIH committees for years, yet with no contact with MRC or Quebec funding committees. My interactions with The Arthritis Society revealed that I was about the only basic scientist involved in my area of arthritis research at this time. As musculoskeletal research in Canada evolved and developed in the late 1980s, in centres like Calgary, London, Toronto and Quebec City, new centres of expertise arose across Canada.

These groups, and many other scientists, both basic and clinical, were brought together by the National Centres of Excellence programs from which we (Tony Cruz, myself and Jeff Dixon - three basic scientists and a clinician scientist- John Esdaile) were able to create the Canadian Arthritis Network (CAN) in 1998. This very successful network lasted for 14 years with periodic competitive peer review approval. Its creation enabled us to change the way arthritis research is done in Canada. We introduced bone and pain researchers and developmental biologists with many other previously uninvolved research specialties to arthritis research. We created multidisciplinary and multi-lab team grants with much more emphasis on advancing knowledge into practical applications rather than just generating it. These programs actively promoted the creation of new partnerships with industry. This was made possible by involving industry early on in the research as an equal partner. We also included patients at every level, guiding and critiquing our programs and peer reviews, sitting on our review and management committees. They in turn connected to patient groups across Canada and acted as a single voice heard by governments.

With the freedom we were given to manage CAN we were able to attract, with great success, outstanding people to work on arthritis. We created enriched graduate training programs that I had previously not seen in Britain. Now they have the outstanding Nuffield graduate studies program. Our new structure caught the attention of those planning the new CIHR operational structure. A similar but much shorter 5 year program was then introduced in Germany with much success.

There is still, to the best of my knowledge, nothing like these large long-term programs in our field in Britain and Europe, nor the USA. Four or 5 year programs exist, but they are too short to achieve meaningful outcomes. It takes time to build such research programs and collaborations as I have again recently experienced. This was with my involvement in helping establish, fund, mentor and guide a four year European Commission Framework 7 program. That closed very recently, just as we were meeting our initial objectives: imaging early molecular degenerative changes in articular cartilages. So frustrating that we could not continue when we had overcome so many hurdles and research progress was becoming impressive. Canada’s 14 year program was truly visionary.

What I did enjoy in Britain were closer relationships between local scientists; afternoon and evening meetings to share and discuss common scientific interests, such as over a meal in college followed by a talk and discussion. Over here I notice less enthusiasm for this outside the lab. We also had very lively and critical discussions and verbal exchanges both in the lab and at meetings. Shortly after I arrived I was critiquing, in question time, a paper presented at a meeting in the states, pointing out some weaknesses. Afterwards I was advised that this didn’t normally happen. People were surprised that I was so outspoken. I presume it was because people were worried that the person being critiqued might one day be reviewing a grant or paper from the critiquer. Back in Britain we never worried about that as it was seen to be part of the scientific process that all accepted – even if it almost came to blows which once happened at a meeting in London, England. Once outside the meeting we were usually all friends again.

I criticized my students and post-docs quite openly at times at lab meetings so that they knew that it was important to be well organized and thorough when presenting and discussing science; that it was intended to help them become better scientists and defend their work with others. And that it was important that they learned how to deal with criticisms. This is what I experienced in Cambridge and it served me well later. I think the system of debate in Canada and USA is still more timid than what I have seen in UK and Europe. I remember one of my students presenting at a European meeting some very innovative work on a new way of detecting the denaturation/ degradation of type II collagen in arthritic cartilage. “It’s all artifact” was the response from a certain well respected European scientist. My student then proceeded to calmly explain why it wasn’t an artefact. The lab sessions had prepared him well!

AG: Please give a summary of your current research activities.

RP: I retired from McGill and Shriners Hospital at the end of 2005 and my laboratory was closed. But I have continued to be involved in research both in Canada, USA, Europe and Japan, working from home. I continue to maintain my interest in developing new biomarkers of growth and onset of arthritic disease and disease activity, in part with IBEX that
Interview with Robin Poole PhD, DSc.

licensed the biomarker technology we developed in my lab from Shriners Hospitals. A new urine assay has been developed by them to detect disease-specific degradation of type II collagen in articular cartilage rather than both physiological and pathological turnover. This is proving very interesting, both in a study with colleagues in Estonia and those in Vancouver. It can detect early onset of osteoarthritis (OA) and its progression: relationships with symptoms and joint function have also been observed. Other new assays based on type II collagen cleavage are being developed.

A collaborative study with colleagues at West Point Military Academy is revealing the ability of the serum assay for type II collagen synthesis to identify people at risk for cruciate ligament damage that can result in subsequent knee OA onset. This could have much value in the area of sports medicine.

In the recent study with colleagues in the European Community Framework 7 program involving 15 partner labs, new nanotechnology is being developed that enables us to start to image, with MRI and tissue targeted SPIONS, molecular damage to cartilage. This permits us to identify early and specific molecular pathologies at source within the joint. This was a very challenging project that I enjoyed from its conception, helping write the proposal, and then helping guide its development and progression.

I also keep busy reviewing papers and funding proposals and chairing scientific advisory boards.

AG: In your opinion, what are the key breakthroughs in cartilage research in the past decade?

RP: The following have caught my attention:

- Recognition of involvement of chondrocyte hypertrophy in degeneration of osteoarthritic (and repair?) articular cartilages.
- Recognition of value of type II collagen degradation biomarkers in detecting and monitoring cartilage degeneration and need for multiple biomarkers with which to monitor cartilage formation and loss.
- Recognition of importance of canonical Wnt pathway and receptor/signalling involvement in TGF beta regulation of both cartilage assembly and degeneration.
- Further elucidation of regulation of chondrocyte formation from stem cells and their subsequent maturation and differentiation.
- Identification of critical importance of superficial layer of articular cartilage and mechanisms that regulate its development.
- Identification of importance of the sub-chondral bone/cartilage junction.
- Improvements in MRI resolution and development of other imaging modalities.
- Increased understanding of structure and molecular interactions and functions of molecules of cartilage extracellular matrix.
- Ability to recreate biological and biodegradable matrices using 3D printing.

AG: What do you feel are the current barriers to successful research in cartilage repair/regeneration?

RP: At the human level, I have always felt that the science in this area has often been too superficial and lacking depth and detail. Not enough in-depth study is being given to the big problems and challenges that exist. There is often what seems like a lack of science involved in many clinical studies. There has to be more integration and collaboration between the basic and clinical sciences in this area. Multidisciplinary research teams are essential because of the complex challenges that we face.

A major critical technical challenge is the integration between new repair tissue and the existing resident tissue. This is a major barrier to success and should be a research priority and focus for future studies. The ability to recreate a true articular surface with all its special properties and great tensile strength is a great need. This is arguably one of the most critical aspects of articular cartilage repair.

Further barriers include:

- The retention of a pre-hypertrophic chondrocyte phenotype. Hypertrophy leads to matrix loss, calcification and cell death by apoptosis. Understanding and appreciating the importance of the microenvironment around chondrocytes and recreating it, is critical. We must remember that in vivo this involves both chemical and mechanical influences.
- Understanding in detail how stem cells can evade or nullify the immune system and thereby escape detection and destruction is another must.
- Creating stem cell lines that can be used from a library for patients in the operating theatre is what is needed for all sorts of tissue regeneration work as well as cartilage.
- Being able to image and identify true hyaline cartilage repair is essential for clinical studies.
- Identifying an animal model(s), the results from which translate into people, is another must.

AG: Is there a particular area where clinicians and researchers should focus their efforts?

RP: Much improved communication and understanding by working more closely together to better understand the problems and how best to solve them. Not enough thought is given to many of problems that we face today. This is obvious in the presentations at meetings on cartilage repair. Multidisciplinary collaborations are essential to solve most, if not all, of the clinical problems we face today.

In terms of cartilage repair, the focus should be on maintaining the chondrocyte pre-hypertrophic phenotype, integration of new cartilage with that already present, and ensuring that a new functional superficial zone is recreated. “It’s mainly about recreating a microenvironment that is permissive for full expression of the pre-hypertrophic phenotype.”

AG: What advice would you give to young researchers, both at the graduate level and young faculty starting their own laboratory?

RP: To all: Be much focused in your research. Work really hard. Keep on top of the literature and earlier work in your
Interview with Robin Poole PhD, DSc.

field. Ensure that you are on top of your methodology. Work on new original projects that advance our knowledge. Do not cut corners. Use methodology that is required but do not get out of your comfort zone by using methods with which you are unfamiliar. At the same time, do not avoid using methods that are important to the study because you are unfamiliar with them. Develop new methods that are needed to ask key questions. Seek instruction or collaboration to learn or incorporate, through collaboration, new methods. Seek mentors with whom you can discuss your ideas, aims, methods and can critique your work and your grant applications and papers, written with time to spare for critiquing. Do not attempt to achieve too much at any one time. Focus on in-depth research. Go for complete studies with quality publications rather than incomplete studies and rushed publications that result in quantity but lack quality. You will be recognized by your peers for the quality and originality of your work, not how much you publish. Write up completed studies in a timely fashion. Make the time for this. Follow the past and present literature within your area of study very carefully and read around it so you can identify to yourself and to reviewers the importance of your work. Do not be driven by your pet technology. Use technology that can help you solve the problem in hand. Use methods carefully and correctly. Go off and learn new key methods if they are to form the core of your research. Do not be afraid to try out new ideas if the opportunity is there. Build collaborations with those with expertise who can complement your own skill sets and who are interested in working in collaboration. The key to a great collaboration is trust and respect. Do not be put off by negative results. Repeat experiments to ensure that they are reproducible.

When starting a lab ensure access to all key equipment that you need. Lead by example. Ensure that graduate students each have their own well-defined project and be available for them whenever they need to discuss experimental design, methods and results. Try and recruit a technician to work with you in a key part of your research. They will enable you to pursue your own research when you are busy with paper work and following the literature. Techs are also invaluable in a teaching role, especially regarding methodology. Do not be put off by failure to get a proposal funded or a paper accepted. This is commonplace now. To be a good scientist you must be very positive and optimistic. It’s your passion and dedication for the research that will carry you forward. Keep knocking on that door. In time it will open easier as you work becomes better known.

AG: Do you have any top tips to run a successful lab?
RP: In addition to the above points outlined above, always be available to your staff. Lead by example with your own project(s). Don’t lock yourself away in your office. Spend plenty of time in the lab, both working on a project and discussing work with colleagues. Your presence will have a positive impact on your colleagues. Watch your budget really carefully on a weekly/monthly basis. Sign all orders so you can review all orders and spending to avoid unnecessary expenditures. Always plan well ahead to ensure that funds (salaries and running costs) are available for students and staff. Realize that you will have to write grant applications on a very regular basis to make this possible. Have a weekly meeting to discuss lab business/problems first (15 min.), then research findings with whole lab. Have one person presenting their research for about 30 min. followed by plenty of discussion and planning for future work. Alternate these meetings with a journal club to discuss new relevant publications. These meetings are of great importance. Have the meetings when your clinical colleagues are available if your work involves basic and clinical studies. Be informal with your colleagues. Let you and your work gain you their respect. Ensure that your trainees receive full acknowledgement for their research at all times and as first authors if it is their project and they have contributed much of the work. Include technicians in the authorship of papers if they made significant contributions, at least of a technical nature.

At lab meetings, ensure that you have a lively and critical discussion of research: that presenters can defend their work and are self-critical. Essential that this happens in a constructive manner. For me, this was extremely important in my growth as a scientist. Defending my findings in the face of often aggressive comments prepared me to be much more thorough and self-critical. It started in Cambridge at the Strangeways. I was often the most critical in Montreal but my trainees and those of others realized it was for their benefit. They knew I was doing this to make them more critical and better scientists and well prepared for the world outside the lab. When trainees became critical of my own work, and for good reason, I knew I had done my job. In other words encourage your colleagues not to accept information at its face value. The latter was the main take-home message for many of my clinical trainees. My lab was more like my other family where I was always available for advice and guidance should this be needed. Nobody was on their own. Avoid recruiting gifted people who cannot get on with others. It can disrupt the whole lab atmosphere and productivity. In today’s multidisciplinary research, team players are really important. Always interview applicants so you can see how they think and what they know and access their personalities. CVs alone can be really misleading. Spend plenty of time with a promising candidate to be sure of your decision. Those with poor first degrees can sometimes become very creative scientists. Try and spot these attributes and provide opportunities to advance their education and offer employment opportunities.

Finally, I feel that it is extremely important to have other interests outside the lab, in my case preferably involving the outdoors and physical exercise. This really helps you recharge your batteries and enjoy your work more when coming back to the lab refreshed. Mine has been rowing and coaching rowing (in UK) and cottage life, cross-country skiing, hiking and birding in Canada.

AG: How do you feel we can improve collaboration between clinicians and basic scientists?
RP: I worked with clinicians all through my career from the time I moved to Cambridge where I started to work on human disease. I spent much time collecting specimens from operating theatres, often being present during surgery. I went to autopsy regularly to collect specimens and in abattoirs col-
Interview with Robin Poole PhD, DSc.

lecking bovine joints and fetuses. Many of my trainees were young rheumatologists and orthopedists. There were always clinicians training in research working in the Montreal and Cambridge labs. These were 2 year post-docs in Montreal, wherever possible. It takes 2 years to get into a project so that you have at least one or two meaningful papers as first author and others as co-authors. This extended experience enabled the clinical trainees to understand research much better and to collaborate more effectively in future research. If they did not pursue a research career themselves they said it taught them to be much more critical of data and less inclined to blindly accept information. I think they became more inquiring and critical in their future day-to-day activities. For collaborations between clinicians and basic scientists to work effectively it is essential that they are equal partners; that planning and results are shared and the clinician is not viewed as a supplier of research material. Set up regular meetings to discuss the research at times that the clinician can be available. Write grants together, publish together and co-supervise trainees together so that it can be seen that this is a true partnership.

AG: Do you have any particular hobbies outside of the lab?
RP: When I was working full time I had little spare time as I found the work and my responsibilities all consuming. I took my reviewing home with me most of the time. But I loved going with the family at weekends to our cottage on a large lake in the mountains in Vermont. That I still do but mainly with my wife. Now I have control over my life (semi-retirement) I spend much more time birding, walking and photographing birds and nature. I love being able to watch premier league soccer by satellite. Being by the water means a lot to me so our homes are on lake/river shorelines. I really enjoy reading, both fiction and non-fiction, especially detective and espionage stories, classics and history. Visiting our children and their families and the grandchildren and relaxing in the garden and countryside are also top of my agenda. But my research was always more of a hobby for me than a job. So I continue my involvement in science at various levels, including research oversight and collaborations, especially in the biomarker area.

AG: Would you, or have you, encouraged your children to get involved in research?
RP: No. I firmly believe that research is something that you can only do well over a long period if you are truly passionate about it. For me it was in my blood before I was even 6 years old. Our children must follow their own passions and dreams. I think I put off my kids from my sort of career and the pace at which I lived it – by what they saw of my great involvement in my work. Only one daughter is involved today in research as a university professor and that is more to do with societal issues and mental health. She returned to academia later in life after working as a social worker for many years. There I admit that I strongly encouraged her to do a PhD so she could open doors that previously remained closed to her. It worked. I got home later than all the other dads and very often had to work on lab related matters at home and at weekends. But I think they all understand me now. I must also add that I have an extremely understanding and supportive wife who enabled me to do what I did. Without her support I would never have been able to do what I did. God bless her. Now we have much more the time to relax and spend together.

AG: Desert Island Disks time! – Two pieces of music, a book and luxury item that you would choose to have with you, stranded on a desert island - and why?
RP: I love all sorts of music from jazz to Led Zeppelin, classic ballads and their female singers, to Amy Winehouse and all sorts of classical music. My classical choice would be Hilary Hahn’s violin concerto in Vaughan Williams’ The Lark Ascending with the London Symphony Orchestra conducted by Colin Davis. I first heard it some years ago driving to visit someone. I found it magical. Such an evocative piece and so beautiful. My other choice, again really difficult, would be Ella Fitzgerald singing Moonlight in Vermont. Besides loving Ella’s wonderful voice and perfect pitch, I so enjoy all the Cole Porter, Irving Berlin and other song classics that she and other female singers of her generation brought to us mere mortals and gave us so much pleasure. Another reason is that we are lucky to have a cottage beside a mountain lake in a very special place – you guessed it – Vermont. The locals call it “God’s little Acre” and so do we. The moonlight over the lake is something very special. Besides, it was the weekend retreats to Vermont throughout the year that enabled me to unwind and be with my family and be fresh for a new week of scientific discovery.

My book choice is War and Peace by Tolstoy. This was the first book I read on my retirement. I had spent almost all my spare time reading scientific papers, which was of critical importance to my work. So I now enjoy this luxury with one book after another coupled with weekly PubMed reviews to keep me in touch with the literature.

My luxury item would be a Porsche sports car. I have always loved driving with the top down since my first car. This was a Triumph Roadster 1800, a convertible that was the forerunner of the TR series. Built in 1946, it had a single bench seat of the TR series. Built in 1946, it had a single bench seat with two “dickey” seats in the rear. I spent many hours working on it to keep it on the road. We had to sell it when our first baby arrived. In 1998 I bought a Mazda MX-5 Miata. I only use it in the summer because of our winters but its real motoring. A new Porsche would be a nice addition.

Thank you for your interest in my life in science. I hope my answers to your questions are of help to our younger colleagues in their exciting scientific voyages into the unknown.
Do’s and Don’ts in the Laboratory

Elisabeth Seebach, Martin Ruetze, Wiltrud Richter, University of Heidelberg and Dobrila Nesic, University of Bern

Do’s
1. Always include the most relevant positive and negative controls in each experiment. Even if all your lab members fully trust your results (there should be at least one who would be reluctant no matter how trustworthy a person you are), the reviewers will not without proper controls!

2. Make sure you work with the right cells.
   • Cell type - identify which cell type (in terms of tissue derivation) is the correct one for the experiment you are setting up. You would not want to mix osteoblasts with alginate beads to produce cartilage, or chondrocytes with hydroxyapatite to make bone, but you may consider using bone marrow MSC for either.
   • Human or animal cells - human material is not easily obtained and for some experiments, animal cells may suffice. However, the relevance for clinics, (i.e. real-world patients), should never be lost from sight!
   • Cell lines or primary cells - cell lines are wonderful creatures because they allow for reproducibility but they are not reflective of normal cells and the results should be confirmed with primary, healthy cells. To be forever dividing, i.e. immortal, they must have acquired a mutation (usually more than one), and more often than not, the mutated gene remains unidentified. Moreover, by being immortal, they are prone to additional mutations (bad tends to get worse) and one really bad cell clone can overgrow and suppress the initial cells. As a consequence, instead of an Anakin Skywalker, you will deal with a Darth Vader (Fig 1.). To avoid Attack of the clones, i.e. Star Wars in your culture, it is a good idea to keep an initial passage of a cell line and cross-check with the one you are currently using. The primary cells are also not without flaw; while they do provide clinically relevant data, large individual variations could make them a sour ally, and you will face many repetitions until reproducibility makes you comfortable with the result.

3. Check for the regulation of your reference / housekeeping genes. Genes are considered as housekeeping as long as they do not respond to treatment – if there is no literature describing the treatment you are about to try - and even if there is, you are better off confirming it - make sure your gene maintains its expression level during the treatment.

4. Estimate how many independent repetitions / donor numbers you need to reach statistical significance before starting your study.

5. When you work in a sterile hood with ethanol to sterilize your instruments by flaming, make sure the beaker with ethanol is far away from the flame!!! And if a drop of flamed ethanol escapes into the beaker, instead of panicking and running out of the lab screaming, cover the beaker to prevent oxygen access.

Don’ts
1. Never make conclusions based on the results of a single experiment. Before you start jumping for joy, or crying your heart out, repeat it at least once (if it is negative), or twice or more (if it is positive) to be sure the results are real.

2. Do not appraise triplicate measurements as three independent experiments. Measuring the weight of 3 mice is not the same as measuring the weight of the same mouse 3 times!

3. Do not compare the gene expression levels of two different genes after quantitative PCR even if you relate them to a reference gene. Primer efficiency is a critical parameter and it may differ from one gene to another.

4. Never rely on the postulated identity or amount of frozen cells obtained from somebody else. It is advisable to get someone with experience to check the cells’ morphology as a first screen on whether you have the right ones. Moreover, trips on dry ice as well as life in liquid nitrogen are very unhealthy for cells; beware that the amount of cells after thawing may substantially decrease due to cell death, and thus do not blindly rely on the cell numbers provided.

5. Avoid methods and assays that create data which cannot be properly verified, like assay kits with reagents of unknown composition or software that processes your raw data with unknown algorithms. Handle “black boxes” with care and validate with a second independent method whenever possible.

For example:
• Do not work with CT or CP values that were calculated by your quantitative PCR software before you have checked your raw data and you know your cDNA amplification was efficient and specific
• Do not rely on deconvoluted images unless you see the same features under the microscope
• Try to find out the basis of the chemical reaction of a ready-to-use assay, and if this reaction is specific for your target; adding “solution A and solution B” to your probe and hoping for a reliable read-out may prove too hopeful!

Figure 1. Attack of the clones!
EDITORIAL

ICRS Newsletter

The ICRS Newsletter is published bi-annually. In case of enquires, comments or if you would like to send us your contribution or adverts, please contact office@cartilage.org

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Deadline for application & submission of an advert and contributions in electronic form:
Summer: April 30
Winter: October 30

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