# Report on the **8th International Conference on Bone Morphogenetic Proteins**

Leuven, September 15-18, 2010

Supported by the **ESF/Remedic Travel Grant Scheme for young researchers**

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## Summary

The biannual 8th International Conference on Bone Morphogenetic Proteins (BMPs), organized in Leuven for the first time, presented according to its strong tradition a multidisciplinary scientific program and hence the complete spectrum of BMP signaling, from bench to bedside. We were very pleased that despite limited funding for travel within many countries and organizations/institutes, there were altogether 253 registrants, with only 7 last-minute drop-outs, thus ending with a total of **246 registrants**, with about 100 registering in a period between -3 and -1 months of the start of the conference. This was in fact the maximum number we could accept, for the most convenient congress facilities in Leuven do not allow a larger crowd (except for one university-based lecture hall, which would have been inconveniently large). The attendants came from 26 countries, 73% from Europe, 17% from the US and another 10% from other countries.

We also received **138 abstracts** for which we intentionally set a late abstract deadline in order to provide the opportunity to the participants to present their most recent work. The abstracts were pre-screened (e.g. for session allocation, and their complementarities and quality) in the last week of August by Luyten/Huylebroeck and then an intense interaction took place with the chairmen of each session who were e-mailed all abstracts, so also the non-preselected ones. Altogether, **47 abstracts were selected for podium presentation** (including of the 8 extra speakers listed below), and care was also taken to provide the podium to researchers in an early stage of their career, and including the high-level participants supported by our ESF/Remedic Travel Grant Scheme (see final program, where these supported speakers are indicated). The vast majority of these selected presentations, together with all other abstracts, were also displayed as posters during the **two poster sessions**. The poster sessions were well attended and very lively and interactive, and they contributed significantly to the success of the meeting. The last-minute selection of podium speakers is a hallmark of the BMP Conferences. The limited number of **17 invited speakers** all delivered top notch presentations. In the final weeks before the meeting, the organizers also selected **8 extra speakers**, based on their strong track record and evident leadership in the BMP field. This resulted in a final total of **62 speakers on 246 registrants** (i.e. speaker:participant ratio about 1:4, poster presenter:participant ratio about 1:2). This was also reflected in an excellent participation to the sessions during the meeting, including on Wednesday afternoon (the starting day) and Saturday morning (the last day of the meeting).

All attendees agreed that the **overall scientific level of the meeting was very high**. In addition, many of the presentations and posters had plenty of new and hitherto unpublished data. The sessions and the conference days were quite heavy but well-attended. Some comments, if any, were about insufficient input/abstracts from the cancer field (BMPs and cancer, including brain gliomas). The clinical session on Saturday morning was well attended but the participation of clinicians, such as orthopedic surgeons and traumatologists, was limited despite the content of this session and the complementarity between the presentations had been very well coordinated between the organizers, the chairs and the speakers.

The organization ran smoothly and very little trouble shooting was necessary. This was confirmed on the lunch meeting on Friday with the International Organizing Committee, to whom the facts and figures of the meeting were presented. The advantage of Leuven, a relatively small provincial University town, is that everything is within walking distance, as was noted by the committee. Also the short distance from Brussels airport was considered an asset.

We can conclude that the meeting, and some of its new additions (like the “Beyond the barriers” talks) in comparison to its previous events, was **a success on all fronts**. The high number of participants for this specialized meeting in times of economical crisis is indicative that there continues to be a need for this type of multidisciplinary meeting in this medically relevant research field.

It is clear that **ESF-REMEDIC** through its substantial and for this meeting unprecedented funding of travel grants for young researchers has contributed significantly to the success of the conference. This support was instrumental and in fact was meeting one of the critical aims of the meeting, i.e. bringing young people in contact with the established investigators in the field. The interaction with ESF staff and with ESF/Remedic on the establishment, the basic concepts and the discussion of the final selection list of awardees of the Travel Grant Scheme was experienced as excellent and very efficient by the local organizers.

In view of all this, the International Organizing Committee decided that the 9th International meeting on BMPs will take place, in 2012, in Davis, California, USA.

## Description of the scientific content and discussions at the event

This conference deals with the complete spectrum of BMP signaling, from bench to bedside. BMPs, known for their bone inductive activity, are involved in many developmental processes that in embryos range from dorso-ventral patterning to organogenesis/tissue specification and the progenitor and differentiated cells in these. BMPs have been shown to play a role in the maintenance of the function of many postnatal tissues including cartilage and bone, but also e.g. kidney, fat, heart and brain. As it becomes clear that mechanisms of postnatal tissue repair and tissue response in disease does encompass reactivation of developmental pathways including BMP signaling, the disciplines covered during this conference are getting broader, and hence they increasingly bring together embryologists and cell biologists, biochemists and molecular biologists in the signal transduction field, human geneticists and other pathologists. In addition, BMP devices are clinically used in skeletal indications such as spine fusion and delayed/non-healing fractures. Product development is ongoing in extra-skeletal disease such as acute and chronic renal injury, osteoporosis and osteoarthritis, and brain trauma. This pathway is (finally) also a major target for drug screeners. As BMP technology comes further to maturation, other potential applications are also emerging such as diabetes and certain types of cancer. The BMP conference therefore continues to appeal to a broad spectrum of researchers, i.e. from hardnosed molecular biologists revealing new molecular mechanisms to hot-shot clinicians reporting new clinical data, presenting a wide overview of recent results in different fields to the participants, and remains quite unique in this respect.

We **started on Wednesday mid-afternoon** with a true bang, somehow as anticipated. A truly outstanding session on **control mechanisms of BMP signalling** (part I) brought several top notch speakers presenting new data on novel regulators, including SNW1 (a nuclear factor controlling BMPRs upstream, and isolated from a gain-of-function expression screen in Xenopus -Caroline Hill, London, UK), SMOC 1 (a secreted matrix protein regulating BMP signaling downstream of the receptor-Malcolm Moos, Bethesda, USA) and TRAF4 (a smurf1/2 interacting cytosolic protein-Peter ten Dijke, Leiden, NL). A comprehensive proteomic approach identified novel smad-interacting proteins, including PAWS1 (Gopal Sapkota, MRC unit, Dundee). Novel smad-inhibitory mechanisms were presented by Lan Xu (University of Massachusetts Medical School, Worcester, USA). Finally, a young investigator from the well-known Katagiri lab (Satoshi Ohte, Saitama Medical University, Japan) reported on the identification of Zranb2, a nuclear protein interacting with R-smads but not smad4. After this session, The **Marshall Urist lecture** was this year delivered by Liz Robertson (Oxford-UK). She gave a truly outstanding and very educational lecture on the role of TGF/BMP signaling in cell lineage commitment in the early mouse embryo, with specific attention to players such as nodal and its complex regulation and downstream targets of nodal such as *Eomes*, and on its turn targets of this T-box protein. It became overwhelmingly clear that the scope and depth of her experimental work over the last two decades contributed very substantially to the field. The Marshall Urist lecture was thus a well deserved recognition for Liz Robertson's contribution to the field.

On **Thursday morning**, a second session continued to discuss the vast field and diversity of **control mechanisms of BMP signaling**. Ye-Guang Chen (Tsinghua Univ, Beijing, China) discussed the use of mouse ES cells to map candidate target gene promoter occupancy by smads. He found an association with a large group of developmental regulators mainly marked by H3K27 trimethylation, repressed in the self-renewing state and induced upon differentiation. He provided convincing evidence and therefore added to the emerging picture that smad-mediated BMP signaling balances self-renewal versus differentiation in stem/progenitor cells, in his case by modulating a set of regulatory genes such as Jmjd3, Dpysl2 and DUSP9. Herb Lin (Harvard Medical School, Boston, USA) gave an almost instructional course on BMP co-receptors, in particular hemojuvelin (HJV), with BMP6 as a key endogenous ligand. He provided strong evidence of the central role of BMP/HJV signaling in the regulation of hepcidin and thus iron metabolism. These two presentations were followed by 15-min presentations of 5 young investigators, some of them attending the meeting with ESF support (see final program). They all presented data on various types of regulatory mechanism of BMP signaling including receptor mobility, BMP endocytosis, intracellular receptor activation, and promoter analysis. It is clear that these new insights will contribute to the development of new chemical compounds modulating BMP signaling, which may provide lead candidates for further drug development.

Session 3 covered **BMPs and developmental biology**, and logically connected to the two previous ones and the Marshall Urist lecture for it is clear that much of our knowledge of the multiple functions and modes of regulation of BMP signaling has emerged from studies in early embryos and in a later phase their developing organs. This was also exemplified by the talk of Paulo Pereira (Leuven), who – at the end of session 2 – provided a smooth transition towards this session 3, discussing how nodal activity in the early mouse embryo is controlled by BMP signalling at the smad2-smad1/5 interaction level. The two invited speakers in session 3 addressed different aspects of BMP signalling in embryos. Irma Thesleff (Helsinki) discussed BMP signalling in the overall paracrine and transcriptional regulation of early tooth initiation, where for example epithelial-mesenchymal reciprocal and reiterated interaction involving BMPs is a key event, as well as later tooth morphogenesis. Through elegant work in conditional knockout mice, An Zwijsen (Leuven) provided for the first time evidence that BMP-Smad1/5 in addition to acknowledged Notch signalling enables an angiogenic vessel to discriminate tip and stalk endothelial cells. Most of the other selected speakers of

this session were acknowledged experts in the field addressing either early phases of mouse development or, again using mice as the main model, development of pathologically relevant organs and/or differentiated cells, including hearts, cranio-facial development and joints.

The **session about BMPs in Musculoskeletal Biology** was an example of how BMP signaling is becoming of relevance for postnatal pathology. Fibrodysplasia Ossificans Progressiva (FOP) is a striking illustration of the impact of BMP signalling in human disease. Eileen Shore (University of Pennsylvania Medical School, USA) illustrated that mutational analysis in the human model are unique opportunities to identify unknown biological functions and mechanisms of action. Novel ACVR1 mutations result in mild hyperactivation of BMP signalling associated with FOP type patients, with features unusual for classical FOP. In line with these findings, Rik Lories (Leuven), the second invited speaker in this session, described the impact of modulation of BMP signalling on more common arthritic diseases with particular attention to these forms of arthritis that display abnormal ankylosis. BMP modulators are indeed potential therapeutic agents to control the process of ankylosis postnatally, a process that is partially uncoupled from inflammation. Catherine Sydall, a PhD student of the Loughlin labs (Newcastle, UK) presented an excellent talk with data on the association of Gdf5 with osteoarthritis, and her studies on trans-acting regulatory factors that are responsible for the observed differential allelic expression of Gdf5. Using a novel proteomics approach, she identified a number of potential regulatory proteins, and more detailed work is in progress. Finally, to extend the relevance of BMP signaling in arthritic diseases, Geri Gross (Braunschweig, Germany) in collaboration with the Montpellier labs (Apparailly, Jorgensen), demonstrated convincingly that the kinase TAK1 is a promising target for inflammatory arthritis. In the last part of this session, several young investigators presented data on improved BMP delivery systems and new aspects of BMP engineering, including the use of heterodimers and biomimetics films, respectively.

New at this conference were the two **"Beyond the barriers" lectures** delivered by Konrad Basler (Zurich, Switzerland) on Thursday night and Thomas Braun (Bad Nauheim, Germany) on Friday night, after the poster session. These were intended to provide food for thought to the BMP research community with regard to new research directions and opportunities with new conceptual insights. Konrad Basler discussed in a meticulous way the role of dpp morphogen gradients in a new aspect of morphogen biology, i.e. organ growth, and how this morphogen can influence the final size of the wing discs in the fly. This lecture left the audience breathless, and the minds of the audience were frantically trying to stay in connection throughout this outstanding and exciting lecture. Questions of the audience were numerous, most notably on the somewhat forgotten role of the extracellular matrix, some proteins of which bind BMPs, in the scenarios presented. Thomas Braun was exemplifying the fact that BMP signaling becomes of major interest in cardiovascular development and pathology, further revealed by the high number of abstracts on BMPs and the cardiovascular system. His work on BMP10, originally (co)discovered by Noreen Cunningham (hence the presence of the Cunningham lecture in the program), and its role in the development of the trabeculated myocardium, is of great interest. This is just a beginning of an era where BMPs/GDFs move into myocardial (and also skeletal muscle) biology and prenatal, pediatric and adult cardiology.

On **Friday**, the broad applications of BMP biology became clear with a first keynote lecture of Slobodan Vukicevic (Zabreg, Croatia), a leader in the BMP field, who discussed the role of BMPs in the regeneration of organs, mainly in soft organs. Applications in kidney disease have become very tempting, but in particular novel BMP formulations to further exploit their therapeutic and regenerative potential are extremely exciting, somehow announcing a new generation of BMP technologies. Gareth Inman (Glasgow, UK) has another BMP favorite, BMP9. He introduced the potential role of BMPs in cancer biology, an aspect of BMP biology that is still relatively unexplored. His findings indicated that BMP9 signaling, probably via a receptor complex containing alk2, may be a novel therapeutic target in ovarian cancer. Other aspects of BMP biology, in particular their role in vascular malformations were discussed by the young investigator Marwa Mahmoud (Newcastle, UK). Impressive were the data presented by the senior biotech scientist (who recently left Pfizer) Vishwas Paralkar. The role of BMP6 as an endocrine regulator of glucose homeostasis is very surprising and novel, and highlights the enormous potential of BMPs in postnatal biology, including as regulators of systemic/endocrine processes in pancreas and liver. These data are a nice example of thinking out-of-the-box, and are pushing the boundaries by doing well-designed in vivo experiments. The role(s) of BMPs beyond bone truly is (are) without limitations and were exemplified with presentations of potential roles in adipogenesis, uterine biology, axonal diseases and cancer.

The **Hot Topics** session on Friday afternoon, started of with an inspiring lecture by Stefano Piccolo. The BMP signalling system, as no other TGF system, is intensively regulated by autoregulation, feedback control and synexpression. The field has thusfar failed to study this in a (quantitative) systems biology type of approach, but S. Piccolo is setting the high standards by his work in the Spemann Organizer and anterior-posterior development of the Xenopus embyo. Using a combination of in vivo experiments and mathematical modeling, he examined a gene network, encompassing BMp components, that regulates the organizer's own antero-posterior architecture, and also confers robustness to organizer patterning by limiting the activity of two opposing ligands, Nodal and ADMP, respectively protecting and repressing head organizer formation. His resulting model of intracellular and extracellular regulations ensures a reliable and fail-safe communication between the trunk and the head organizer, enhancing robustness of head induction in the

frog embryo. This session was further mostly focused around BMP modulation, with particular attention on small molecules. Paul Yu (Boston, USA) discussed the development of small molecule BMP inhibitors, and their potential applications. Alexander Bullock (Oxford, UK) reported on the ongoing work on structural analysis of the activation of the BMP receptor ACVR1 in FOP, and the identification of new chemical inhibitors with a potential for therapeutic development. Crystal structure studies led indeed to the identification of a new class of kinase inhibitors with some receptor specificity, which is probably a critical aspect to allow clinical development/use of inhibitors of BMP/TGF signaling.

Session 7 covered **BMPs in the context of stem cell biology and tissue regeneration**. Christine Mummery (leiden, NL) discussed the role/potential of stem cells as a platform for human disease models and new drug discovery. She particularly focused on Human Hereditary Telangiectasia models, elaborating on the underlying mutations in endoglin, a non-signalling co-receptor for TGF, and the work done in different systems to address underlying mechanisms of action. A series of mostly young investigators subsequently presented data on the role of BMPs in adipogenesis, and hematopoiesis, with description of role of the stem/progenitor cells in this regard. Ugo Ripamonti (Johannesburg, South Africa) reported on the particular role of BMP7/OP1 in cementogenesis and periodontal ligament regeneration. Esmeralda Blaney-Davidson, a young investigator from Nijmegen, reinforced the importance of balances in TGF/BMP signaling and the impact this has on joint and cartilage biology.

The **Clinical session on Saturday** morning clearly reinforced the opinion that there is ample space for new 2$^{nd}$-generation BMP technologies, and that the surgical community has to take its responsibility with respect to the further positioning of BMP devices in clinical practice. The state of the art lecture of Enrique Gomez-Barrena was very instrumental to make this last point, and indicated the challenges we face in clinics today with respect to bone healing and how to position the BMP devices in clinical practice. There is no doubt that BMP technology is on the forefront of “orthobiologicals”, a new and growing industry, but much work in the clinic has still to be done. Peter Giannoudis (Leeds-UK) further reinforced this. He discussed clinical algorithms and the so-called diamond concept, i.e. focusing on both the biological and mechanical environment in the individual patient. New BMP delivery systems and technologies were proposed by Ulf Wikesjö (Goteborg, Sweden) and Ernst Hunziker (Bern, Switzerland). W. Carlson (from Thrasos) presented data on novel BMP peptide agonists of BMP signaling.

The **closing session on Saturday** morning **further expanded the role of BMPs beyond bone**. In a well-prepared and most inspiring presentation, Thomas Willnow (Berlin, Germany) highlighted the importance of tight regulation of BMP signaling in yet another system, i.e. adult neurogenesis, from the progenitor cell zone in the lateral ventricle of the forebrain. LRP2 appears to be a clearance receptor for BMP4, and this novel mechanism of LRP2-mediated catabolism of BMPs is critical in this adult neurogenesis system. A surprising and novel aspect of BMP biology, preciously suggested but now becoming of importance, is the role of BMP1 and its isoforms. L. Grgurevic (Zagreb, Croatia) demonstrated that the MP1-3 isoform systemically regulates kidney function, providing a novel therapeutic target.

The **Noreen Cunningham** lecture was presented by Petra Knaus (Berlin, Germany). She gave a top overview lecture discussing dynamics in BMP signaling. She beautifully illustrated that amongst others recent advances in technologies have allowed us to gain new insights in the diversity of BMP signal transduction mechanisms. She made it crystal clear that BMP technology, and the multiple regulations of BMP signalling, is still in its infancy. Major breakthroughs in particular with respect to therapeutic opportunities in regenerative medicine will only be possible through in-depth understanding of the molecular cues driving the pleiotrophic effects of BMPs. There could not have a better message to finish this exciting BMP Conference.

## Assessment of the results and impact on future directions

It is fair to state that the BMP conference in Leuven was a true success on all fronts. Very positive comments and feedback from members of the International Organzing Committee and – importantly – also participants from all levels in their career have been received during and after the conference.

***Organization****:*

- No major issues/problems did come up. Mostly exclusively positive feedback on the local organization team has been received, as well as sincere congratulations for the local organization, which had decided not to involve a professional congress organizer for reasons of high cost. Several critical aspects that were major assets to this success such as the conference website (and its continuous updating), the on-line registration system and the on-line credit card paying system, and our way of hosting and providing assistance to the invited speakers, were communicated to the board for future reference.
- Advertisement in major journals such as Nature are very costly and probably – as seen from the fluxes of received subscriptions in function of time and comparison with the two publication dates in Nature - not

worthwhile in the future. It is likely better to use an updated version of our about 1200 functional e-mail addresses to spread the news on future events in the field.

- A recognized major asset to the success of the meeting, and at the same time a completely new aspect of the meeting, was the support by the ESF-Remedic Travel Grant Scheme that we established in coordination with the ESF staff. Since there is limited corporate funding for a field that is still mostly research and development, and a program that is driven by the quality of the submitted abstracts, this support was instrumental in attracting young fellows from abroad, including EU fellows working in the USA. 32 grants were awarded, essentially supporting almost all young investigators that applied, although their abstracts and cv's had been ranked by the organizers first.

***Format of the meeting:***

- We believe that the present sessions, and also the new "Beyond the barriers" lectures, and the poster sessions, and their location and timing, were well received. The program turned out a bit heavy but the overall feedback was very positive. Attendance to the sessions was excellent, with good discussions. Not everybody is supposed to attend everything, thus there are no major changes required to the format. Another asset of the meeting venue was also the possibility to follow the talks live in another big well-equipped room (with desks etc) located next to the lecture hall, enabling some participants to withdraw from the main hall and giving them the opportunity to work and access the internet etc and thereafter return to the main hall.
- The posters sessions were lively, well attended, and the posters were of very high quality, both in terms of presentation/discussion and content. The poster awards (selected by a committee, given on Saturday night during the conference dinner, were well deserved and highly appreciated.
- A 4-day meeting starting on Wednesday afternoon and finishing on Saturday evening is indeed the most appropriate format, enabling overseas scientists to leave on Sunday morning. No changes were recommended.
- The selection of most speakers based on the abstracts and their quality has inevitably some risk, but turned out to have worked out very well. Inviting a limited number of speakers, with some discretionary possibilities for the organizing committee to adjust the program and speakers in function of scientific developments, should be maintained as the model to organize this conference in the future.

***Novel tendencies and future directions in the field:***

- BMP signaling becomes very relevant to postnatal tissue homeostasis and pathology, with very exciting findings in new disease areas including diabetes, kidney and cardiovascular disease, possibly skeletal muscle repair, and in chronic arthritis. The involvement of BMPs in systemic processes including glucose homeostasis is beyond the expectations of even the most visionary minds.
- Major steps forward in basic science with regard to regulation of BMP signaling, understanding of which is critical if one seeks to develop therapeutic applications. Developmental systems with strong genetics are ideal to address these questions.
- Growing number of potential clinical applications leading to increasing investment and interest in the development of BMP modulators, including agonists and antagonists. This conference has seen new classes of small compounds as BMP regulators, as well as the potential of peptidomimetics. That is what made us decide to dedicate in the Hot Topics session a lot of attention to these small compounds.
- BMP technologies and the new generation products, provide a first glance of the novel wave of new regenerative medicine approaches with particular attention on orthobiologicals, but extending clearly in the field of stem cell biology and tissue engineering.

**Conclusion:**

- We are truly looking forward to the 9$^{th}$ International Conference on BMPs in Davis, California, USA, 2012, and we are convinced we have given with the Leuven meeting a new boost to the BMP Conferences.
- Thanks a bunch to the ESF/REMEDIC support! Without this support, this meeting would not have been possible.

# 8th International Conference on Bone Morphogenetic Proteins

Leuven, September 15-18, 2010

## Wednesday, September 15, 2010

*Jubileumzaal, University Hall,1st floor (Naamsestraat 22, 3000 Leuven)*

From 12:00 till 17:30 Registration
*Jubileumzaal, 1st floor*

**Start of the meeting**
*Promotion hall,University Hall, 1st floor*

15:15 – 15:30 Welcome
**Frank P Luyten** and **Danny Huylebroeck,** local organizers

**Session 1: Control mechanisms in BMP signaling, part 1** (Kohei Miyazono (was not able to come) / Petra Knaus)
*Promotion hall, University Hall, 1st floor*

15:30 – 16:00 **Caroline Hill** (London) (A5)
SNW1 IS A CRITICAL REGULATOR OF SPATIAL BMP ACTIVITY AND NEURAL
PLATE BORDER FORMATION IN VERTEBRATE EMBRYOS

16:00 – 16:20 **Malcolm Moos** (Bethesda) (A6)
AN EXTRACELLULAR MATRIX-ASSOCIATED BMP ANTAGONIST

16:20 – 16:40 **Peter ten Dijke** (Leiden) (A7)
REGULATION OF TGFbeta/BMP SIGNALING BY TRAF4

16:40 – 16:55 **Gopal Sapkota** (Dundee) (A8)
UNDERSTANDING THE MOLECULAR MECHANISMS BY WHICH BMP SIGNALLING IS REGULATED

16:55 – 17:10 **Lan Xu** (Worcester, MA) (*A9)
A NOVEL SMAD INHIBITION MECHANISM MEDIATED BY THE STE20 KINASE MISSHAPEN

17:10 – 17:25 **Satoshi Ohte** (Saitama) (*A10)
IDENTIFICATION AND CHARACTERIZATION OF A NUCLEAR PROTEIN AS A CO-SUPPRESSOR OF BMP-REGULATED R-SMADS

17:25 - 17:45 ***The European Science Foundation***
**Maria Manuela Nogueira** (Strasbourg)
THE EUROPEAN SCIENCE FOUNDATION (ESF) AND THE RESEARCH NETWORKING PROGRAMME "REGENERATIVE MEDICINE" (REMEDIC)

17:45 – 18:00 **Welcome by Mark Waer**, Rector of KULeuven

18:00 – 19:00 ***Marshall R. Urist lecture***
*Introduction by Hari Reddi*

**Elisabeth Robertson** (Oxford) (A1)
TGFβ SIGNALING PATHWAYS GOVERNING CELL LINEAGE COMMITMENT IN THE EARLY MAMMALIAN EMBRYO

19:15 – 20:15 Reception/welcome by Mr Louis Tobback, Mayor of the city of Leuven
*City Hall Leuven*

20:30 – 22:30 Walking dinner
*Jubileumzaal, University Hall, 1st floor*

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## Thursday, September 16, 2010

*Provinciehuis, Provincieplein 1, 3000 Leuven*
*Auditorium 'Vlaams-Brabant'*

**Session 2: Control mechanisms in BMP signaling, part 2** (John Wozney / Peter ten Dijke)

08:30 - 09:00 **Ye-Guang Chen** (Beijing) (A11)
GENOME-WIDE ANALYSIS OF SMAD TARGETS REVEALS THE ROLE OF BMP SIGNALING IN MOUSE ES CELL FATE DETERMINATION

09:00 – 09:20 **Herb Lin** (Cambridge, MA) (A12)
THE CENTRAL ROLE OF THE BMP CORECEPTOR HEMOJUVELIN IN THE REGULATION OF IRON METABOLISM

09:20 – 09:35 **Asja Guzman** (Berlin) (*A13)
IMPACT OF BMP RECEPTORS´ LATERAL MOBILITY ON SIGNALING

09:35 – 09:50 **Hamed Alborzinia** (Heidelberg) (*A14) *with ESF support*
KINETIC ANALYSIS OF BMP-2 ENDOCYTOSIS

09:50 – 10:05 **Alex Bullock** (Oxford) (*A15)
STRUCTURAL INSIGHT INTO ALK2 R206H MUTATION AND INHIBITOR DESIGN FOR FOP

10:05 – 10:20 **Francesca Giacopelli** (Genova) (*A16)
STUDY OF THE ACVR1 GENE EXPRESSION AND REGULATION: THE PROMOTER REGION AND THE 5'-UTR

10:20 – 10:35 **Paulo Pereira** (Leuven) (*A17)
BMP/SMAD5 SIGNALING ANTAGONIZES NODAL SIGNALING: A MECHANISM TO PREVENT ECTOPIC PRIMITIVE STREAK FORMATION IN MOUSE

*10:30 – 11:00* *Coffee and tea*
*Spoor 95, coffee corner and hall*

**Session 3: BMPs in developmental biology** (Danny Huylebroeck / Malcolm Moos)

11:00 – 11:30 **Irma Thesleff** (Helsinki) (A28)

REGULATION OF TOOTH INITIATION AND MORPHOGENESIS BY BMPS

11:30 – 11:50 **An Zwijsen** (Leuven) (A29)
BMP-SMADS ARE CRITICAL REGULATORS OF BLOOD VESSEL PLASTICITY AND AMNION HOMEOSTASIS IN MOUSE EMBRYOS

11:50 – 12:05 **Yuji Mishina** (Ann Arbor) (A30)
BMP SIGNALING THROUGH ACVR1 IS CRUCIAL FOR ESTABLISHMENT OF THE LEFT-RIGHT ASYMMETRY VIA PROPER FORMATION OF NODE CILIA IN THE MOUSE

12:05 – 12:20 **Vesa Kaartinen** (Michigan, MI) (A31)
RIGHT VENTRICLE AND OUTFLOW TRACT DEVELOPMENT ARE DEPENDENT ON BMP TYPE I RECEPTOR ALK2 (ACVR1) EXPRESSION BY SECOND HEART FIELD CELLS

12:20 – 12:30 **Emma de Pater** (Rotterdam) (*A32) *with ESF support*
INHIBITION OF BMP SIGNALING BY SMAD6 IS REQUIRED FOR TERMINAL DIFFERENTIATION OF VENTRICULAR CARDIOMYOCYTES

12:30 – 12:45 **Dawn Clendenning** (Nashville, TN) (*A33)
INTERACTIONS BETWEEN GDF6, BMP4, AND NOGGIN IN CRANIAL SUTURE AND SKELETAL DEVELOPMENT

12:45 – 13:00 **Petra Seemann** (Berlin) (A34)
INHIBITION OF GDF5 BY NOGGIN IS REQUIRED FOR JOINT DEVELOPMENT

*13:00 – 15:00* *Lunch Spoor 95*

**Session 4: BMPs and musculoskeletal biology** (Frank Luyten / Kenneth Bloch)

15:00 – 15:30 **Eileen M. Shore** (Philadelphia, PA) (A41)
MILD HYPER-ACTIVATION OF BMP SIGNALING IN VARIANT FORMS OF FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

15:30 – 15:50 **Rik Lories** (Leuven) (A42)
THE DIFFERENT FACES OF BMPS IN CHRONIC ARTHRITIS

15:50 – 16:00 **Catherine Syddall** (Newcastle) (*A43) *with ESF support*
FUNCTIONAL ANALYSIS OF THE OSTEOARTHRITIS (OA) ASSOCIATED VARIANT rs143383

16:00 – 16:15 **Geri Gross** (Braunschweig) (*A44)
SYSTEMIC RNAI-MEDIATED SILENCING OF TAK1 IS A NOVEL AND EFFICIENT THERAPEUTIC APPROACH FOR RHEUMATOID ARTHRITIS

*16:15 – 16:45* *Coffee and tea*
*Spoor 95, coffee corner and hall*

16:45 – 17:00 **Robert Martinez** (Cambridge, MA) (*A45)
BMP-2/6 HETERODIMER IS MORE OSTEOGENIC THAN BMP-2 AND BINDS STRONGLY TO BOTH THE TYPE L AND TYPE LL RECEPTORS

17:00 – 17:15 **David de Gorter** (Leiden) (*A46) *with ESF support*
BIPHASIC EFFECTS OF TGFBETA ON BMP-INDUCED OSTEOBLAST DIFFERENTIATION

17:15 – 17:30 **Thomas Crouzier** (Grenoble) (*A47) *with ESF support*
THIN BIOMIMETIC FILMS OF CONTROLLED STIFFNESS AND BIOACTIVITY AS AN INNOVATIVE TOOL TO UNRAVEL BMP-2 EFFECTS ON CELLULAR PROCESSES

17:30 – 19:00 **Poster session 1** (participants present posters with uneven numbers)
*Spoor 95*
Belgian beers

19:00 – 19:30 **Extra lecture "Beyond the barriers"**
*Introduction by Danny Huylebroeck*

**Konrad Basler** (Zurich) (A2)
DPP, GRADIENTS AND GROWTH

*Free evening*

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## Friday, September 17, 2010

*Provinciehuis, Provincieplein 1, 3000 Leuven*
*Auditorium 'Vlaams-Brabant'*

**Session 5: BMPs beyond bone, part 1** (Kuber Sampath / Jody Haigh)

08:30 – 09:00 **Slobodan Vukicevic** (Zagreb) (A54)
REGENERATION OF ORGANS BY BMPS

09:00 – 09:20 **Kohei Miyazono** (Tokyo) (A55)
EFFECTS OF BMP ON VASCULAR ENDOTHELIAL CELLS AND IDENTIFICATION OF TARGET GENES

09:20 – 09:35 **Gareth Inman** (Dundee/Glasgow) (A56)
PRO-PROLIFERATIVE BMP9 SIGNALLING

09:35 – 09:45 **Marwa Mahmoud** (Newcastle) (*A57) *with ESF support*
MECHANISMS UNDERLYING THE DEVELOPMENT OF ARTERIOVENOUS MALFORMATIONS IN TWO INDUCIBLE MOUSE MODELS OF HEREDITARY HAEMORRHAGIC TELANGIECTASIA

09:45 – 10:00 **Vishwas Paralkar** (New London, CT) (A58)
A NOVEL ROLE OF BMP6 AS AN ENDOCRINE REGULATOR OF GLUCOSE HOMEOSTASIS

10:00 – 10:15 **Caterina Clementi** (Houston, TX) (*A59) *with ESF support*
BMPS AND UTERINE BIOLOGY: THE ROLES OF BMP TYPE I RECEPTORS IN THE PERI-IMPLANTATION PERIOD

10:15 – 10:30 **Evan Reid** (Cambridge, UK) (A60)
UPREGULATED BMP SIGNALING: A COMMON PATHOGENIC MECHANISM FOR AXONAL DEGENERATION?

*10:30 – 11:00* *Coffee and tea*
*Spoor 95, coffee corner and hall*

**Session 6: BMPs: Hot Topics** (Caroline Hill / Hari Reddi)

11:00 – 11:30 **Stefano Piccolo** (Padova) (A85)
PATTERNING WITHIN THE SPEMANN ORGANIZER: A GENE NETWORK FOR ANTERO-POSTERIOR SPECIFICATION

11:30 – 11:50 **Paul Yu** (Boston, MA) (A86)
APPLICATIONS OF SMALL MOLECULE BMP INHIBITORS IN PHYSIOLOGY AND DISEASE

11:50 – 12:05 **Julia Zimmer** (Berlin) (*A94) *with ESF support*
BMP2 VARIANTS WITH REDUCED BMP ANTAGONIST SENSITIVITY FOR IMPROVED REGENERATIVE POTENTIAL

12:05 – 12:15 **Roberto Ravazzolo** (Genova) (*A88)

THE ROLE OF THE 3'-UTR REGION IN THE REGULATION OF THE ACVR1 GENE EXPRESSION

12:15 – 12:30 **Jan Boergermann** (Berlin) (*A89) *with ESF support*
DORSOMORPHIN AND LDN-193189 INHIBIT BMP-MEDIATED SMAD, P38 AND AKT SIGNALLING IN C2C12 CELLS

12:30 – 12:45 **Jennifer Heinke** (Freiburg) (*A90) *with ESF support*
BMP MODULATOR BMPER IS HIGHLY EXPRESSED IN MALIGNANT TUMORS AND CONTROLS INVASIVE CELL BEHAVIOR

12:45 – 13:00 **Olexandr Korchynskyi** (Amsterdam) (A91)
TIEG1 AND TWIST1 INTEGRATE PROINFLAMMATORY AND BMP EFFECTS ON THE SKELETON AND BRAIN FORMATION

*13:00 – 15:00* *Lunch* Lunch Meeting of the Organizing Committee
*Spoor 95* *Klein Rijsel*

**<u>Session 7: BMPs, stem cells and tissue repair</u>** <u>(Irma Thesleff / Christine Mummery)</u>

15:00 – 15:30 **Christine Mummery** (Leiden) (A95)
PLURIPOTENT STEM CELLS AS CARDIOVASCULAR DISEASE MODELS

15:30 – 15:40 **Ugo Ripamonti** (Witwatersrand, Parktown) (*A103)
THE INDUCTION OF CEMENTOGENESIS AND PERIODONTAL LIGAMENT REGENERATION BY BONE MORPHOGENETIC/OSTEOGENIC PROTEINS IN NON-HUMAN PRIMATE MODELS

15:40 – 15:50 **Yu-Hua Tseng** (Boston, MA) (*A97)
BMP7 DRIVES BROWN ADIPOGENESIS IN TISSUE RESIDENT PROGENITORS

15:50 – 16:00 **Mihaela Crisan** (Rotterdam) (*A98) *with ESF support*
ROLE OF BMP4 AND HEDGEHOG FACTORS DURING HEMATOPOIETIC DEVELOPMENT IN MOUSE EMBRYO

16:00 – 16:10 **Steven Goossens** (Gent) (*A99) *with ESF support*
SIP1 IS ESSENTIAL FOR MURINE EMBRYONIC HEMATOPOIETIC STEM/PROGENITOR CELL DIFFERENTIATION AND MOBILIZATION

*16:10 – 16:40* *Coffee and tea*
*Spoor 95, coffee corner and hall*

16:40 – 16:50 **Shirley Motaung** (Pretoria) (*A100)
INDUCTION OF EXPRESSION OF SUPERFICIAL ZONE PROTEIN (SZP) IN MUSCLE-DERIVED MESENCHYMAL PROGENITORS/STEM CELLS BY TGFbeta-1 AND BMP-7

16:50 – 17:10 **Esmeralda Blaney-Davidson** (Nijmegen) (*A101) *with ESF support*
SMAD2/3 SIGNALING IS CRUCIAL FOR CARTILAGE MAINTENANCE, WHEREAS SMAD1/5/8 SIGNALING DETERMINES CHONDROCYTE TERMINAL DIFFERENTIATION

17:10 – 17:20 **Vladimir Botchkarev** (Boston, MA / Bradford) (*A102)
OVEREXPRESSION OF SMAD1 IN THE SKIN IMPAIRS POSTNATAL HAIR CYCLING, WOUND HEALING AND PREVENTS TUMOR FORMATION VIA FUNCTIONAL RESTRICTION OF EPITHELIAL STEM CELLS

17:20 – 17:30 **Laurent Obert** (Besancon) (A135)
PRELIMINARY PROSPECTIVE MONOCENTRIC COHORT TO EVALUATE THE SAFETY AND THE EFFECT OF RH BMP7 IN RESISTANT LONG BONE NON UNION

17:30 – 19:00 **Poster session 2** (participants present posters with even numbers)
*Spoor 95*
Belgian beers

19:00 – 19:30 **Extra lecture "Beyond the barriers"**
*Introduction by Frank Luyten*

**Thomas Braun** (Bad Nauheim) (A3)
SIGNALING IN THE SPECIFICATION MYOCARDIAL LAYERS AND THE REMODELING OF THE CARDIOVASCULAR SYSTEM

*Free evening*

# International Conference on Bone Morphogenetic Proteins

Leuven, September 15-18, 2010

## Saturday, September 18, 2010

*Provinciehuis, Provincieplein 1, 3000 Leuven*
*Auditorium 'Vlaams-Brabant'*

**Session 8: Clinical applications** (Ugo Ripamonti / Johan Lammens)

08:30 – 09:00 **Enrique Gómez Barrena** (Madrid) (A114)
BMPS IN TRAUMA AND ORTHOPAEDIC SURGERY: PRESENT AND FUTURE

09:00 – 09:20 **Peter Giannoudis** (Leeds) (A115)
TREATMENT OF LONG BONE NON-UNIONS WITH BMPS

09:20 – 09:40 **Ulf Wikesjö** (Göteborg) (A116)
COMPARATIVE STUDY OF BMPS AND DELIVERY STRATEGIES

09:40 – 09:55 **Ugo Ripamonti** (Witwatersrand, Parktown) (A117)
THE INDUCTION OF BONE FORMATION BY BMPS IN NON-HUMAN AND HUMAN PRIMATES

09:55 – 10:10 **Ernst Hunziker** (Bern) (A118)
THE IMPORTANCE OF THE MODE OF GROWTH-FACTOR DELIVERY IN BMP-2-INDUCED BONE-TISSUE ENGINEERING

10:10-10:25 **William Carlson** (Quebec / Boston, MA) (A119)
NOVEL PEPTIDE AGONISTS OF BMP SIGNALING: A POTENTIAL THERAPY FOR PROGRESSIVE RENAL FIBROSIS IN CHRONIC KIDNEY INJURY

*10:25 – 11:00* *Coffee and tea*
*Spoor 95, coffee corner and hall*

**Session 9: BMPs beyond bone, part 2** (Slobodan Vukicevic / Vishwas Paralkar)

11:00 – 11:30 **Thomas Willnow** (Berlin) (A61)
LRP2 PROMOTES ADULT NEUROGENESIS THROUGH SUPPRESSION OF BMP4 SIGNALING

11:30 – 11:40 **Lovorka Grgurevic** (Zagreb) (A75) *with ESF support*
BONE MORPHOGENETIC PROTEIN (BMP)1-3 ISOFORM OF BMP1 GENE CIRCULATES AND REGULATES KIDNEY FUNCTION

11:40 – 12:15 **Noreen S. Cunningham lecture**
*Introduction by Hari Reddi*

**Petra Knaus** (Berlin) (A4)
DYNAMICS IN BMP SIGNALING – DYNAMICS IN BMP RESEARCH

*Lunch (lunch bags available)*

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## Social program during the free afternoon

*Vouchers needed*

Excursions
All buses leave from Provinciehuis
12:45 departure to Bruges - bus leaves from Bruges at 17:00
13:00 departure to Ghent - bus leaves from Ghent at 17:15
13:30 departure to Brussels - bus leaves from Brussels at 17:45

20:00 Conference Dinner
*Faculty Club*