

Transgenic Technology meeting 2008 in Toronto, Canada: a meeting report

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Abstract In a history that goes back to 1999, the Transgenic Technology meetings started out in Sweden and over the years began to attract a growing community of technicians and researchers mainly from Europe. As the meetings started to attract an expanding worldwide audience, the community decided to found the International Society for Transgenic Technologies at the Barcelona meeting in 2005. The 2007 convention was held at Brisbane, Australia, and in 2008, the 8th Transgenic Technology meeting was held for the second time on behalf of ISTT and for the second time outside of Europe in Toronto, Canada. Due to its excellent program with over 400 participants the meeting was able to attract the highest number of delegates of all past TT meetings. With extended times for plenary discussions about technical and organizational aspects, as well as top level scientific presentations, both technicians and scientists enjoyed this as an extremely fruitful meeting from which they could take home solutions for daily routines as well as new insights and ideas for coming projects.

Keywords Transgenic · Knock-out · Genetic modification · Meeting · Transgenic Technology · North America · Canada

The meeting started with welcome addresses by Lluís Montoliu on behalf of the International Society for Transgenic Technologies (ISTT, www.transtechsociety.org) as well as the organizers Kristina Vintersten and Andras Nagy. This was followed by addresses in memoriam to Charles Babinet (Lluís Montoliu) and Anne McLaren (Andras Nagy). Both were excellent scientists, who made major contributions to the field of Transgenic Technology with their work over decades. It was perceived as a great loss to the community that these two great mentors and researchers had passed away this year.

The first session of the meeting was dedicated to stem cell research and early embryology. Janet Rossant (The Hospital for Sick Children Research Institute, Toronto, Canada) gave an overview of community resources such as gene targeted and trapped ES cell clones and RNAi libraries. In addition, she discussed the use of totally ES-derived fetuses and lentiviral transgenesis. Then Davor Solter (Max-Planck-Institute for Immunobiology, Freiburg, Germany) discussed the use of chimeras and transgenics for the study of development, which included fascinating experiments, where embryos with two paternal or two maternal pronuclei were generated. Due to health reasons Andzej Tarkowsky (University of Warsaw, Poland) could not attend the meeting but Andras Nagy presented an outline of his work on his behalf. Dr. Tarkowski is seen as one of the founding fathers of embryo technology. Throughout his work he has shown a broad area of interests including

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interspecies hybrids, nuclear reprogramming, parthenogenesis, embryo fusion and experiments addressing the developmental potential of separated blastomeres. The session was closed by Derek van der Kooy (University of Toronto, Canada), who showed how transgenic mice could be utilized in somatic stem cell research and who presented the characterization of a stem cell population that can give rise to neural as well as pancreatic cell lineages.

In the second session, Lluís Montoliu presented Brigid Hogan (Duke University, North Carolina, USA) as the winner of this year's ISTT prize on Transgenic Technologies (sponsored for the sixth time by genOway). In her lecture Dr. Hogan reported on work that utilizes combinations of conditional reporter knock in lines, transgenic lines expressing fluorescent proteins and inducible cre transgenic lines to trace cell lineages in the developing lung. It was fascinating to see how different tools could orchestrate the visualization of specific lineages depending on the timing of their induction and their combination. Moreover, she shared technical details of her studies, a fact that was much appreciated by the audience of the Transgenic Technology meeting.

The second day of the conference featured two sessions with lively round table discussions that were received with the greatest approval. Questions from the audience triggered several in depth discussions. Session III covered basic techniques and was initiated by four presentations on the topics of embryo transfer, vasectomy and cesarean section (Elisabeth Williams, University of Queensland, Brisbane, Australia), ES cell culture and derivation (Sagrario Ortega, National Center of Oncology Research, Madrid, Spain), DNA and ES-cell injection (Johannes Wilbertz, Karolinska Institute, Stockholm, Sweden), and artificial chromosome-type transgenes (Lluís Montoliu, National Center of Biotechnology, Madrid, Spain). For session IV Marina Gertsenstein (Toronto Centre for Phenogenomics, Toronto, Canada) and Elisabeth Williams presented their transgenic units and then engaged into a spirited discussion with two more panelists (Tom Fielder, University of California, Irvine, USA and Thom Saunders, University of Michigan, Ann Arbor, USA) and the delegates.

After lunch, Geoff Hicks (Manitoba Institute of Cell Biology, Winnipeg, Canada) kicked off session V with a talk titled "High-throughput production of

mutant mice". Dr. Hicks presented the NorCOMM initiative that together with other initiatives (EuCOMM, KOMP and TIGM) has set out to generate knock out alleles of all mouse genes. Ann Flenniken (Samuel Lunenfeld Research Institute, Toronto, Canada) showed some examples of phenotypes generated by single point mutations caused by chemically induced single base pair alterations using ENU as a mutagen. She could show how this phenotype-driven approach offers the possibility to expose novel genes and pathways and reveal critical functional domains of proteins. Furthermore, Dr. Flenniken described the challenge of finding the one critical base pair change that would cause the phenotype observed. The Pleiades Promoter Project presented by Elizabeth Simpson (University of British Columbia, Vancouver, Canada) is an effort to generate knock in mouse lines for the research of brain development and disorders. To this end mini-promoters are designed in silico to produce (in a subsequent step) mouse lines that express reporter or cre transgenes knocked into the *hprt* locus with a defined brain-region and cell-type specific pattern. The final speaker of this session was Thom Saunders, who reported on integration and expression efficiencies in BAC transgenic mouse lines and could show that BAC transgenes—if carefully prepared and injected at adequate concentrations—can produce transgenic mice with almost the same frequency as "normal" transgenes.

Session VI covered cutting edge Transgenic Technologies. Robin Lovell-Badge (MRC National Institute for Medical Research, London, UK) started with a presentation of how to study cell fate and the roles of genes, presumed to play a role in stemness or stem cell niches. In his studies, these questions are approached with the help of targeted null and conditional alleles and transgenic mice. PDGF signaling was in the center of Philippe Soriano's (Mount Sinai School of Medicine, New York, USA) lecture. In his extensive and highly interesting studies, Dr. Soriano used gene targeting and transgenesis, including gene trap approaches in mice, to learn about the functions of several target genes of the pathway, with the common phenotype that their mutations cause male or female infertility. Gordon Keller (McEwen Centre for Regenerative Medicine, Toronto, Canada) gave the conference participants an insight into differentiation patterns of embryonic

stem cells and showed for populations that could give rise to hematopoietic and vascular lineages that these run in parallel in murine and human development. The aim of these studies is, as Dr. Keller explained, to gain the ability to utilize ES or induced pluripotent stem (iPS) cells in cell replacement therapy, developmental biology, drug discovery and testing, and in modeling human disease. Andras Nagy (Mount Sinai Hospital, Samuel Lunenfeld Research Institute, Toronto Canada) followed up with a two-part presentation, starting out with the discussion of the pitfalls of stable expression of transgenes both in (ES) cell culture and in vivo and how to navigate around those traps. In the second part he presented the NorCOMM gene targeting strategy, the toolbox researchers could utilize when working with mice harboring this construct and how the ϕ C31 integrase can be used to vary the targeted locus.

The last day of the meeting started with session VII that was entitled “Phenotyping”. The first presentation, given by Mark Henkelman (The Hospital for Sick Children, Toronto, Canada), demonstrated the multitude of imaging techniques the Toronto Mouse Imaging Centre (MICE) has to offer. These range from possibilities to scan live mice using magnetic resonance tomography or ultrasound imaging to optical and X-ray based techniques that can only be applied to a fixed specimen. Dr. Henkelman showed fascinating high resolution pictures of adult mice and embryos that have proven to be of great value in the analysis of disease models and developmental phenotypes. A further method to study cardiovascular phenotypes in mutant mice was demonstrated by Lee Adamson (Mount Sinai Hospital, The Samuel Lunenfeld Research Institute, Toronto, Canada). In her work she uses highly developed techniques to study the cardiovascular system of female mice and their offspring during pregnancy and after birth. To this end micro-ultrasound, Doppler ultrasound, electron microscopy, and X-ray imaging are used and permit the detailed evaluation of cardiovascular phenotypes. In the following talk, Colin McKerlie (Toronto Centre for Phenogenomics, Toronto, Canada) gave a mind-boggling review of the Toronto Centre for Phenogenomics (TCP) with its animal holding units with their robotic cage change management, research and imaging areas, pathology and behavioral analysis set-ups as well as its cryopreservation possibilities and

transgenic core facility. The next talk of the session was Junji Takeda (Osaka University, Osaka, Japan), who reported on the generation of bi-allelic mutations in murine ES cells that could then be used to generate homozygous null mutants via the generation of chimeras with tetraploid embryos. Dr. Takeda described how he used Bloom deficient cells that show a highly increased ratio of chromosomal crossing over to generate homozygous mutant cells with high frequency. Using this technique Dr. Takeda was able to identify Ronan, a suppressor of Nanog, in a screen for ES cells that would retain stemness without the addition of LIF to the culture medium. The final talk of the session was by Simon-Pierre Demers (University of Montreal, Canada), who reported on the generation of rat ES-like cell lines that he demonstrated to be multipotent in vitro as well as in vivo. Following this route Simon-Pierre Demers hopes to be able to generate genuine rat ES cells in the near future.

The closing session of a very successful and inspiring TT2008 conference was opened by Tom Fielder (University of California, Irvine, USA), who introduced the transgenic facilities survey that has been initiated by the ISTT following his proposal. The survey is currently running and aims to define standards in the generation of transgenic and chimeric mice that transgenic facilities could use as goals when improving their techniques and in discussions with clients. More information can be found on the ISTT website at www.transtechsociety.org. Then I as the organizer of the next TT meeting had the opportunity to introduce the Max-Delbrueck-Center for Molecular Medicine (MDC) as the venue for TT2010 that will be held in Berlin, Germany, March 22–24, 2010. I will be happy to welcome you and your colleagues to the MDC!

The ISTT has received a number of letters of thanks for a great meeting. However, we owe the organizers a debt of gratitude, above all Kristina Vintersten, Marina Gertsenstein and Andras Nagy, for a great meeting with lots of new information, broad space for discussion and good opportunities to get together with international colleagues.

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