

The University of Texas M. D. Anderson Cancer Center
in conjunction with the
International Society for Transgenic Technologies

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER



Advances in Transgenic Animal Research
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MEETING REPORT



As the first ISTT-sponsored meeting in North America, the recent event at the M. D. Anderson Cancer Center (MDACC) in Houston, Texas, was an unqualified success, with 204 attendees from all over the world. The MDACC, which is visited by some 80,000 cancer patients yearly, is part of an amazing complex of medical centers, hospitals, research institutes, clinics, and universities, located about 5 miles from downtown Houston.

The meeting kicked off with registration and an evening social, accompanied by posters and vendor displays, on Friday, January 11. Attendees were welcomed Saturday morning by Jan Parker-Thornburg, principal organizer and assistant professor at MDACC, William Klein, chairman of the MDACC Department of Biochemistry and Molecular Biology, and ISTT President, Lluís Montoliu.

Saturday and Sunday talks were divided into two Plenary Sessions, four Sessions of related talks, and two forums consisting of brief presentations followed by roundtable discussions.

In the first Plenary Session, Gigi Lozano of MDACC described mouse models developed in her laboratory to elucidate the actions of negative regulators of the tumor suppressor protein, p53. This was followed by a series of talks centered on mouse genetics, including a description of coat color genes and 129 strain differences by Ana Perez of Taconic and a tour of the Mouse Genome Informatics website by Teresa Chu of the Jackson Laboratory. The session concluded with a discussion of the importance of genetic background by Fernando Benavides of MDACC.

The theme for Saturday's forum was ES cell culture and blastocyst injections. Jennifer Alana (MDACC) and Thomas Dechiara (Regeneron Pharmaceuticals) described procedures and outcomes for two variations on the standard technique of injecting ES cells into blastocysts to produce chimeric mice, one using cryopreserved embryos and the other using laser-assisted injection of 8-cell embryos. (The XYClone laser used by Regeneron was also available for hands-on demonstration sessions throughout the meeting.) The third talk in this forum was presented by Jun Cheng of NIH, who described the use of defined serum-free media to improve the efficiency of deriving C57BL/6 ES cell lines. The three speakers then fielded questions from the audience.

Following the forum session, ISTT travel awards were presented to Elizabeth Hughes of the University of Michigan, Ming Xu of the University of Louisville, and Larry Johnson of the University of Alabama, Birmingham.



The Saturday afternoon session focused on alternative transgenic strategies. First up was Thom Saunders, who described work by the University of Michigan's Transgenic Animal Model Core to refine the technique of making transgenic rats. Thom's team has refuted several myths about rat transgenesis, showing for example that it can be at least as efficient as making transgenics with C57BL/6 embryos.

Chuan-Wei Jang (MDACC) continued the rat theme with a talk on the use of the PiggyBac transposon system to mediate rat transgenesis. This was followed by two presentations on the use of lentiviral vectors. Oded Singer of the Salk Institute for Biological Studies discussed the delivery of shRNA with lentiviral vectors, and Shirley Pease of the California Institute of Technology described the methods used by her team and David Baltimore's lab to make the first transgenic mice using lentiviral vectors.

Lluís Montoliu of the Centro Nacional de Biotecnología in Madrid, Spain, discussed the use of large constructs, such as bacterial artificial chromosomes (BACs) and yeast artificial chromosomes (YACs), to help ensure proper transgene expression. Lluís's group has pioneered the use of ICSI-mediated YAC transgenesis to improve the efficiency of producing founder animals compared to standard microinjection of YACs.

In the final talk of this session, Kader Thiam of genOway reported on the use of RNAi-mediated gene knockdown to validate drug targets. Using a knockin strategy with the HPRT or ROSA26 loci in ES cells allows more reliable prediction of knockdown success *in vivo*, and this technology is now being extended with the Cre/lox system to produce inducible gene knockdown.

After a long day of intellectually stimulating talks, the Saturday evening dinner social was a welcome respite, featuring great food, good wine, and delightful conversation.

Sunday's Plenary Session speaker was Richard Behringer of MDACC, who entertained the audience with tales of capturing bats and wallabys to study genes involved in development and organ morphology. He described research on the *Prx1* locus in which enhancer sequences of the mouse were replaced with those from a bat, resulting in elongated forelimbs, suggesting that mutations in non-coding regulatory sequences can be a source of evolutionary differences in morphology.

The theme for Sunday's morning session was "Large Scale Knockout Projects and Resources for Targeted ES Cells." Attendees were dazzled by accounts of the progress of various teams, such as the International Gene Trap Consortium (IGTC) and NIH's Knockout Mouse Project (KOMP) to target every gene in the mouse genome, as described by Pieter de Jong of Children's Hospital Oakland Research Institute (CHORI), William Shawlot of the Texas Institute for Genomic Medicine (TIGM), and Wojtek Auerbach of Regeneron Pharmaceuticals.

The last speaker of this session was a person who needs no introduction to ISTT members, namely Peter Sobieszczuk, founder of the Transgenic-List. Peter treated the audience to a tour of various on-line resources, including the IGTC website, the Federation of International Mouse Resources (FIMRe), and the Homo Sapiens Genome View on NCBI's Entrez Genome site. Peter concluded with an update on the Transgenic-List itself. All of the links from his presentation are posted at the list's home page.

Sunday's roundtable forum included presentations by Tom Fielder of the University of California-Irvine on surviving pathogen outbreaks, Lela Riley of University of Missouri's RADIL on infectious agents that can be found in or on mouse ES cells and pre-implantation embryos, and by Jan Parker-Thornburg on the effects of housing conditions on breeding success. The roundtable questions generated some lively discussion of the efficacy of current techniques used to rederive infected mouse strains.

The Sunday afternoon session focused on cryopreservation techniques. Stanley Leibo (University of New Orleans), who has taught many of us how to cryopreserve mouse embryos through the Jackson Laboratory cryopreservation course, discussed vitrification techniques. Steve Sansing of Charles River Laboratories described the implementation of a cryopreservation and recovery program. Carlisle Landel (Thomas Jefferson University) discussed current techniques of mouse sperm cryopreservation and presented results from his efforts to identify genetic loci that mediate the efficiency of sperm cryopreservation.

The cryopreservation session was capped off by a much-anticipated presentation by Charles Ostermeier of the Jackson Laboratory, describing the new sperm cryopreservation technique pioneered at Jax that has been shown to dramatically improve the efficiency of recovering live mice from frozen sperm. Key points of this technique include a specific cooling rate, use of a reducing agent, monothioglycerol, in the cryoprotective medium, and a specific warming rate. This technique is now being taught by Jax and a paper describing it in detail should be published soon.

Jan Parker-Thornburg and her co-organizer, Jennifer Anderson, should be commended for putting together an impressive meeting, with talks ranging from cutting edge technology, to basic biology, to the nuts and bolts of running transgenic core facilities, following the formula that has made all ISTT meetings to date so valuable to the attendees.



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