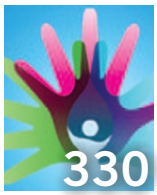
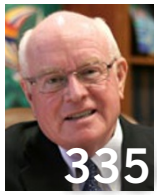


Raring to go:
A survey of rare disease–focused drug companies



Venture forth:
Drug approval vindicates 'venture philanthropy'

Give it a rest:
Diagnosing disease with resting-state fMRI scans

NIH accused of being overly literal on stem cell approvals

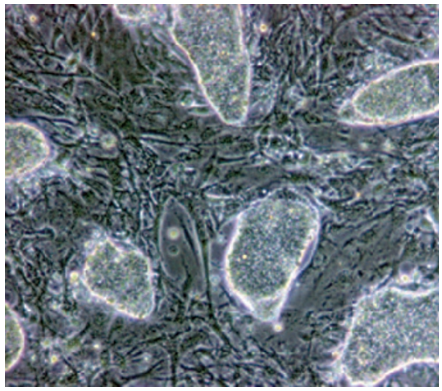
In 2009, soon after the US National Institutes of Health (NIH) established a framework for researchers to submit their human embryonic stem cells (ESCs) to the newly established registry of cell lines eligible for agency funding, Andras Nagy, a senior scientist at Mount Sinai Hospital in Toronto, quickly filed the paperwork for his two creations: CA1 and CA2, the first ESCs derived in Canada. Two years later, in December of last year, the NIH added Nagy's lines to the agency's growing list of those that can be used in US taxpayer–backed research projects.

The approval, however, came with a catch: the cell lines are eligible for funding only at Canadian affiliates of the Canadian Stem Cell Network (CSCN). Notably, only around 0.25% of the NIH's total extramural research budget is spent north of the border, slimming the chances of agency support for the Canadian cell lines even further.

"It's really unintended and quite unfortunate," says CSCN scientific director Michael Rudnicki, a regenerative medicine researcher at the Ottawa Health Research Institute in Ontario. "It was never envisioned that [the consent forms] would be interpreted as precluding use in other jurisdictions."

At the time the lines were created, in 2003, no federal laws existed in Canada for what to include in the consent forms signed by donors of embryos for stem cell research. So, in an attempt to highlight that any resulting cell lines would be used by researchers outside of his own laboratory, Nagy added a sentence to his forms specifying that "[t]he stem cell lines created may be distributed to other Canadian laboratories affiliated with the Canadian Stem Cell Network for further research or potential clinical use."

Nagy says he simply wanted to underscore the benefits that embryo donation could have for all of the country's biomedical research community, especially with Canadian Parliament debating legislation at the time to regulate work with ESCs. Unfortunately, the NIH officials interpreted this sentence "very literally," notes CSCN deputy scientific director Janet Rossant, a developmental biologist at the Hospital for Sick Children in Toronto and part of the scientific management team of the International Stem Cell Initiative, which published the first comparison of CA1 and CA2 together with 57 other lines from 16 other laboratories (*Nat. Biotech.* **25**, 803–816, 2007).


Andras Nagy

Stuck north of the 49th: The CA1 stem cell line.

Even though Nagy maintains that it "was never our intent to limit the distribution of our lines," the NIH took a precautionary stance and interpreted the 'may' as 'may only', thereby making the cell lines off limits for US researchers except through collaborations with Canadian colleagues. "It's very hard to catch all the downstream fallouts from one little phrase," notes Joseph Laning, senior director of the University of Massachusetts Medical School's Human Stem Cell Bank and Registry in Worcester.

True to form

Ren-He Xu, director of the University of Connecticut Stem Cell Core in Farmington, thinks the biomedical agency made the right decision. "It's better to be conservative than to have some infringement," he says. Yet, many others in the field argue that the NIH is acting overly cautiously. The consent forms "didn't say 'limited to or only in Canada,'" notes Bartha Maria Knoppers, director of the Centre of Genomics and Policy at McGill University in Montreal. "So, strictly speaking—in terms of acting in good faith—nothing would have prevented the NIH from distributing [the stem cells] internationally, but they chose to interpret [the forms] on a very narrow scale."

The decision regarding the Canadian lines mirrors previous moves by the NIH to approve ESCs on the condition that any federally funded research is consistent with the language from the informed consent documents. For example, some lines, including a couple dozen from Douglas Melton's lab at Harvard University in Cambridge, Massachusetts, can be used only for studying diabetes, whereas others are limited to characterizing genetic defects and developing new methods for transforming stem cells into other cell types.

"What's lost in all this is the intention of the donor," says Melton. "It's exceedingly unlikely that a donor would say, 'I only want Canadian scientists to use these lines, because the intent for donors is usually, 'I want to find cures for diseases.'" He adds: "It would be nice if that [NIH] board thought more about the donors' intent and the mission of the NIH and were less concerned about what opponents of ESC research might use as an objection."

Story Landis, director of the US National Institute for Neurological Disorders and Stroke and head of the NIH Stem Cell Task Force, defends the agency's decision-making process. "We are being remarkably conservative here because of our desire to not compromise our ability to support human embryonic stem cell research," she says.

For his part, Nagy says that he added an explicit reference to the possibility of worldwide distribution to the consent forms he uses back in 2004, soon after he realized the imprecise wording, and he is now in discussions with NIH officials about loosening the restrictions on the Canadian lines to meet the spirit of the donors' consent. Since their creation, Nagy's cell lines have been requested by more than a dozen Canadian labs but only two groups in the US, according to Michael Hanna, Mount Sinai's business development manager. All along, however, "our aim has always been to make these lines available for the widest possible research community," says Nagy.

Elie Dolgin