Distribution of hESC Lines: How, When, and Where

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Introduction

Little attention has been paid to how national governments with widely divergent policy positions produce segmented markets for human embryonic stem cell (hESC) research, innovation, and product development. This segmentation may have strong and possibly negative effects on American research and economic competitiveness. Does national policy generate country-specific discoveries, intellectual property and therapies? Which countries or regions will emerge as technological or bio-industrial leaders? Will America play a major or minor role?

At the heart of these questions is determining which hESC lines go where. Exchange and transfer of biological materials through material transfer agreements (MTAs) is a regular feature of how science gets done and is often essential for many research collaborations. Cell lines and their reagents are the "coin of the realm" for hESC research—starting materials needed to answer essential biomedical questions.

We are in the process of obtaining raw data describing the number of MTAs initiated and executed by the University of Wisconsin's Wisconsin Alumni Research Foundation (WARF) and from Harvard University, including what lines are being requested and distributed, how many are being distributed, and to what countries the lines are being distributed.

We are particularly interested in hESC lines from these two sources for a few reasons, including:

The WARF lines are approved for US federally funded research while the Harvard lines are not.

Until recently the availability of the WARF lines included a licensing fee while the Harvard lines have been distributed at only the cost of shipping the material.

Methods

Obtaining the data

Launching the project required discussion with stakeholders at WARF and Harvard. We are near the end of working out an agreement under which data will be obtained. Because five institutions have been involved (Harvard, HHMI, Stanford, University of Michigan, and WARF), reaching a final agreement has taken time.

Preliminary data

Studies have suggested that national policy can influence how and what stem cell research is being conducted, and by whom. Owen-Smith and McCormick (Nat Biotech 24, 2006) demonstrate a significant gap in rate of hESC publications between the United States and the rest of the world, over time, and that this trend is on a trajectory of continuing. Levine (Nat Biotech 24, 2006) has shown that US stem cell scientists are 5 times more likely to receive job offers from abroad - many from permissive countries - more so than other biomedical scientists.

Other analyses indicate the countries such as China and India are increasingly targeting biomedical research efforts toward stem cell research (Murray and Spar, NEJM 355, 2006; Salter, Cooper, Dickens, and Cardo, Regenerative Med 2, 2007).

Preliminary data show that between 1998 and 2004, the number of MTAs executed by WARF went from 0 per year to 100 per year, with the numbers increasing almost four-fold between 1999 and 2000 and almost three-fold between 2000 and 2001.

Since Harvard has begun distributing their lines in early 2004, 93 MTAs have been executed domestically. These cover the distribution of 536 lines. There have been 135 MTAs executed with international entities, and these represent the distribution of 636 lines.

Data requested

Examples of data requests:

We have requested the raw data describing the number of MTAs initiated and executed by the University of Wisconsin's Wisconsin Alumni Research Foundation and from Harvard University.

Specifically, by year:

-Date the draft MTA initiated
-Date of fully executed agreement
-Date lines are shipped
-Number of cell lines distributed
-Type of cell line(s) distributed
-Fee associated with the shipped line(s)
-Country shipped to

Both Harvard and WARF keep track of MTAs initiated but not carried to completion. We have requested data on these as well.

Specifically, by year:
-Request date
-Country of request
-Number of lines requested
-Type of cell line(s) requested

We have also requested:

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-Examples of the MTAs executed
-Time points for changes in price of cell lines
-Time points for changes in institutional policy

Data Comparisons

Assumptions:

-Distribution of lines over time is becoming more global
-Distribution of lines is trending away from the United States
-Demand and distribution is increasing in permissive vs. non permissive countries
-Price and policy changes will influence distribution of cell lines

Analysis:

A descriptive, quantitative analysis will be conducted using the information we obtain from WARF and Harvard. Different comparisons include:

-Compare between the two different organizations the total number of MTAs per year.

-Compare the country distribution per year per line.

-Compare institution type (academic, other non-profit, for-profit) distributed per year per line.

-Compare over time: what line to what institution type and in what country.

-Compare MTAs issued per line per year to lines cited in publications per year.

-Overlay price and institutional policy changes with number of MTAs per year.

-Overlay permissive versus non-permissive hESC national policies with comparison of country distribution of cell lines.

-Examine relationship of price, quality, negotiation terms, and country of licensee to the rate of distribution.

Discussion and Future Directions

We anticipate our analyses to reveal which countries and types of institutions are pursuing hESC research, whether demands for lines are increasing or decreasing, whether lines generated in US laboratories stay in the US, and whether investigators are switching from one cell line to another (e.g. presidential to other lines). This landscape of hESC research might suggest what nations are likely to be leaders in this area of research and indicate to national policy makers whether resources ought to be directed to hESC research, if the goal is to be a leader in the field.

In addition, our data might demonstrate that some lines are being requested and distributed more frequently, thus suggesting variance in usability of different lines, both between the two sets of lines and within each set. A comparison MTA data with publication records might suggest how materials are being exchanged, e.g. formally, informally, collaborations, etc. Given the current US regulatory environment for stem cell research, this might be insightful to administrators responsible for providing training to researchers about institutional policies.

Our expectation is that our initial examination of the data will lead to more questions and further analyses. We plan to conduct interviews with researchers, identified through publication data and publicly accessible websites, who have used either or both the Harvard lines and the WARF lines. These interviews will be focused on researchers' perceptions of the material transfer process, the different cell lines available, and the role of IP in hESC research.