LETTERS

Edited by **Jennifer Sills**

Precision medicine: Look to the mice

BY ALL ACCOUNTS, President Obama's Precision Medicine Initiative (PMI) promising molecular-guided diagnostics, therapeutics, and prevention strategies is eliciting enthusiasm and excitement among clinicians, translational researchers, and patients ("NIH plots million-person megastudy," J. Kaiser, In Depth, 20 February, p. 817). To make this hope reality, the PMI Working Group of the Advisory Committee to the Director (ACD) of the National Institutes of Health (NIH) is holding workshops with stakeholders to discuss and resolve critical issues and challenges before launching NIH's $200 million in funding initiatives later this year. Key to the PMI's success is how to gather, manage, and interpret for clinical benefit the unprecedented amounts of genomic, metabolomic, and other –omic data generated by the planned 1 million plus–person research cohort (*1*). There are many facets to this question, including: the advantages and disadvantages of holding patient data in federated and/or centralized databases; standardization of data generated by multiple testing regimens; deriving data both from electronic health records as well as metadata pertaining to environmental influences; ensuring access to and availability of patient data and information that is sufficiently deidentified to uphold privacy rights; curation and other data manipulation to ensure that data is organized and assembled into a format conducive to secondary and tertiary analyses; and sharing of data with national and international research groups.

Many of the issues regarding data management, accessibility, and interpretation first confronted the mouse research community in the Knockout Mouse Production and Phenotyping (KOMP2) project. KOMP2 was established as part of an international consortium [International Mouse Phenotyping Consortium (IMPC)] to provide a comprehensive description of function for each of the more than 21,000 protein coding genes in the mouse genome. Approaching 4 years into a planned 10-year NIH Common Fund timeline, KOMP2 and its global partners are using a common set of phenotyping tests covering 10 organ systems on sex-balanced cohorts of knockout mice (*2*). This process is similar to how the PMI will examine

multiple cohorts of male and female patients according to an agreed-upon set of clinical assays across a broad spectrum of organ systems and disease phenotypes.

From a data management perspective, KOMP2 is now accomplishing in mice what the PMI seeks to accomplish in people. KOMP2 is successfully implementing collaborative solutions to address challenges with phenotyping data from globally distributed cohorts of mice. Biologists, software engineers, and research staff are working together to standardize data through harmonization of test protocols and identification of critical metadata. Access to results is facilitated by central curation of data, transparent statistical analysis, and real-time public posting of curated data from a central website (www.mousephenotype.org) (*3*). (Granted, the absence of privacy and informed consent concerns makes this process simpler for mice than for human studies.) Furthermore, our data meet guidelines for reproducibility of biomedical animal studies (*4*), and our statistical analysis platform is freely available for others to use (*5*).

In addition to data management, results from KOMP2 can provide substantial insight to inform the PMI's effort to define a new molecular taxonomy (*6*). Because we remain largely ignorant of the multiple functions of genes within the mammalian genome, revealing pleiotropy (one gene affecting multiple seemingly unrelated traits) will generate vital new information on genes and disease (*7*). Undoubtedly, many variants of unknown significance will be identified in the PMI 1 million–person cohort. As a majority of genes to be studied by KOMP2 have little or no functional data, our ongoing studies are enabling discoveries beyond what we already know (*8*), revealing essential new knowledge to guide interpretation of the PMI studies planned in humans. As we journey together into this brave new world of precision medicine, we encourage and welcome cooperation of the PMI with KOMP2/IMPC.

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Sexism discussion misses the point

TIM HUNT'S RECENT comments on women in science were incredibly inappropriate (*1*). However, as the response has ballooned into a public discussion excoriating pervasive sexism and discrimination among male scientists (*2*), I find myself bewildered by this message.

Personally, the senior male mentors in my life have bent over backwards to advance not only my research and career, but also my mental health and my work-life balance. Although there are certainly men in the sciences who hold negative stereotypes of women, science is a generally socially progressive community. Even Hunt himself seems to have largely been a strong mentor and supporter of women in science (*3*). If he represents the tail end of the distribution for sexism in science, that is a happy reflection of where the mean lies.

By blaming poor male mentors, and focusing our communal attention on a few egregious comments, we are distracting ourselves from a real opportunity to call attention to much more substantial institutional and structural burdens to women

in science. It is an unfortunate biological reality that child-bearing age for women coincides nearly perfectly with the age when scientists' research productivity needs to be the highest. Yet most institutions have woeful basic childcare available, no support for urgent or extended childcare during work-related obligations, inadequate support for maternity needs, financial disincentives to PIs for hiring postdoctoral fellows with children needing insurance coverage or those who are likely to need maternity leave, no insurance coverage for fertility treatment for women who choose to delay reproduction for career reasons, and little way to account for delays in productivity due to time spent in childcare in the faculty hiring process.

This discussion also inadvertently sends a dangerous, and largely untrue, message to young female scientists that they are still likely to be viewed differently and as lesser than their male counterparts. This undermines the confidence of young women and risks becoming a self-fulfilling prophecy.

Although it is fun to attack outspoken sexist outbursts, we can't let this distract us from the more substantial problem at hand: addressing the shortcomings of our scientific institutions to address the many substantial, if mundane, barriers that still impede women from reaching full equality in science.

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Chimpanzees deserve their freedom

SUSAN LARSON THINKS that keeping extraordinarily cognitively complex chimpanzees locked up for years with interaction with only one conspecific, stimulated by tearing magazines and playing with plastic airplanes, is all right ("The scientist behind the 'personhood' chimps," D. Grimm, In Depth, 12 June, p. 1187). That her prisoners are "collaborators" and "willing participants in the project" is a narrative she may need to believe, but we do not.

Larson mistakes our demand that chimpanzees be recognized as "persons" (i.e., an entity with the capacity for a legal right) eligible for habeas corpus relief for a demand they be treated as "people," when the Nonhuman Rights Project actually demands that they be treated as chimpanzees. She claims that she and her team "don't do anything with these chimpanzees that we haven't done on ourselves," when she hasn't locked herself in a cage with one conspecific for 6 years with newspapers to tear and plastic airplanes to manipulate.

Larson's is a voice from a faded era; because the U.S. Fish and Wildlife Service recently reclassified chimpanzees as "endangered" and the National Institutes of Health refuses to fund chimpanzee research, it may be the last such voice we will ever hear.

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TECHNICAL COMMENT ABSTRACTS

Comment on "Expectations of brilliance underlie gender distributions across academic disciplines"

Donna K. Ginther and Shulamit Kahn

Leslie *et al.* (Reports, 16 January 2015, p. 262) concluded that "expectations of brilliance" explained the gender makeup of academic disciplines. We reestimated their models after adding measures of disaggregated Graduate Record Examination scores by field. Our results indicated that female representation among Ph.D. recipients is associated with the field's mathematical content and that faculty beliefs about innate ability were irrelevant.

Full text at http://dx.doi.org/10.1126/science.aaa9632

Response to Comment on "Expectations of brilliance underlie gender distributions across academic disciplines"

Andrei Cimpian and Sarah-Jane Leslie

Ginther and Kahn claim that academics' beliefs about the importance of brilliance do not predict gender gaps in Ph.D. attainment beyond mathematics and verbal test scores. However, Ginther and Kahn's analyses are problematic, exhibiting more than 100 times the recommended collinearity thresholds. Multiple analyses that avoid this problem suggest that academics' beliefs are in fact uniquely predictive of gender gaps across academia.

Full text at http://dx.doi.org/10.1126/science.aaa9892