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In February 2007, Dean Martin convened an Advisory Committee to examine the current state and future of human genetics at Harvard. Initially, seventeen faculty from across the University (see appendix) held a wide-ranging discussion. After several meetings Dean Martin charged a sub-committee (the authors of this memo) to develop a proposal for future growth based on these discussions.

In September, 2007 Dean Flier charged the subcommittee with evaluating and comparing several specific options, resulting in a report submitted on January 14, 2008. That draft was distributed to, and subsequently modified based upon, comments received (a) from the Human Genetics Advisory Committee, (b) at a meeting of the HMS Preclinical Chairs on January 15, 2008 and (c) from a meeting of the Steering Committee of the Dean's Strategic Planning Process on February 8, 2008.

Current state of human genetics at Harvard

All aspects of health and disease have a genetic basis, and rapidly advancing tools have transformed human genetics research. New discoveries provide great opportunities to reduce human suffering and enhance healthcare. Human genetics has broad implications not only in the sciences, but for law, business, public policy and society. Thus, human genetics is truly an interdisciplinary area of training and research. Harvard and its affiliated institutions have pioneered many of these advances. There is a great need for education related to human genetics at all levels (undergraduate, graduate and professional). It is truly important that we get this right.

Definition

The Committee began by defining “human genetics” for the purposes of our discussions. Human genetics is intertwined with many disciplines, in particular genetics, genomics, clinical medicine, evolutionary biology, epidemiology and statistics. Nonetheless, we felt it a mistake to fully consider the breadth of these disciplines, as we might overreach, and fail to produce practicable suggestions for enhancing human genetics at Harvard.

We defined “human genetics” more narrowly for the purposes of our discussions: as the study of human genotypic variation and its influence on human phenotypic variation. Phenotypic variation includes diseases and other clinical traits, non-medical physical and behavioral characteristics, and responses to the environment, lifestyle and therapy. This definition includes population genetics, disease gene mapping, identification and study, genetic epidemiology, and translation into clinical medicine. Human geneticists require a range of studies in cell and animal models as surrogates for human specimens.

Human genetics is intrinsically multi-disciplinary: individual research studies require deep and simultaneous engagement of basic (laboratory and computational), clinical and

population-based approaches. Human geneticists depend on methods that are rapidly evolving and expensive, and patient populations that are costly and time-consuming to assemble. Human genetic research raises important ethical issues regarding informed consent and privacy. These characteristics weighed heavily in our discussions.

Strengths of the current Harvard model

All agreed that human genetics is strong at Harvard, with many truly outstanding faculty and programs. Harvard's faculty includes leaders in clinical care of patients with genetic diseases, genetic and genomic methods, statistical and population genetics, informatics, and disease research. Our clinical investigators have assembled unmatched patient collections and epidemiological cohorts.

We consider it a great strength that Harvard's faculty in human genetics is not restricted to one department, school, or institution, but is distributed widely. Leaders in human genetics have primary faculty appointments in HMS Department of Genetics (many of whom reside in affiliated hospitals), in clinical departments at each of the hospitals, at HSPH, and at FAS. Faculty and students at other Harvard schools study the impact of human genetics on business, policy, law and society.

We benefit from major research institutes and centers including Harvard Partners Center for Genetics and Genomics (HPCGG), Broad Institute of Harvard and MIT, and MGH Center for Human Genetic Research. These activities offer unmatched capabilities for genetic research. HPCGG has established core facilities and the Laboratory for Molecular Medicine, a molecular diagnostics laboratory. Broad is the nation's leading center for DNA sequencing and SNP genotyping, funded as a National Genotyping Center by NCRR and NIH Gene Environment Initiative. These units possess superb staff, many world leaders in their own rights, and attract substantial funding to the Harvard system.

The multi-focal nature of human genetics means that our expertise and activity are integrated across Harvard and its affiliated hospitals. Each unit has a different focus, with many on a single school or site (at HMS, HSPH, or a single hospital such as Childrens Hospital through its Genetics Division and Genomics Program). HPCGG is a joint effort of Partners and HMS, and Broad spans Harvard, the hospitals, MIT and Whitehead. Some are departments, with responsibility for hiring and promotion (with formal processes for appointments) as well as teaching and research; others are research centers with porous boundaries, but lacking appointment power or formal roles in education.

Each unit contributes to community building across its institutional base. Most have journal clubs and research presentations for members. Weekly meetings of the Broad Program in Medical and Population Genetics are attended by 80 human geneticists from across Harvard. HPCGG hosts an annual conference on Personalized Medicine and sponsors an award for a young investigator in human genetics. MGH's CHGR sponsors weekly research presentations on basic and clinical research from across the hospital.

Harvard hospitals care for patients with genetic diseases, and HMS has one of the oldest training programs in medical genetics that offers clinical training at several of the major

affiliated hospitals. This program has been expanded to several HMS wide joint training programs that involve Medicine, Pathology and Pediatrics.

Limitations of the current Harvard model

The success of the current model, which is based on institutional and organizational diversity, also leads to certain challenges. We discussed many issues, ranging from perceptions of different units, to which institution gets credit for discoveries by our faculty, to whether “the whole is less than the sum of the parts”. In the end, five key issues emerged that we felt were most important in designing a future for the field.

- Recruiting and retaining the world’s leading faculty in human genetics
- Attracting great students and fellows, and offering the best education, in our field
- Translating human genetics discoveries that directly bear on human health
- Articulating needs with regard to shared infrastructure for human genetics
- Supporting the human genetics community across Harvard

Recruiting and retaining the world’s leading human genetics faculty

Faculty recruitment is of central importance, and yet our current structure creates challenges: the lack of critical mass of human geneticists to serve on search and promotion committees and as mentors; the complexity and political nature of recruitments, with recruits receiving competing offers from different parts of Harvard; the highly varied nature of job offers at Harvard; and the perception by some recruits that Harvard is an internally competitive rather than cooperative environment.

A critical issue is that appointments in the HMS quadrangle and FAS are hard money with start-up funds and without limit of time tenure; positions in clinical departments often lack some or all of these features. There is great variability in the packages offered to recruits by the affiliated hospitals. As much recruitment takes place in the hospitals, and as human geneticists are avidly recruited by other institutions, an inability to offer competitive packages can place Harvard at a disadvantage. Some felt that faculty not appointed in an HMS quadrangle department are viewed as second-class citizens, and that this perception was a barrier to recruitment in clinical departments.

Attracting the best students and fellows, and offering the best training

The lack of a pre-doctoral training program in human genetics may make potential students less likely to recognize Harvard’s strength in the field, and less likely to apply for study. The lack of a formal curriculum means that we offer few classes in the discipline, nor a plan of pedagogy. The lack of coordination among the human genetics faculty means that physician trainees seeking postgraduate training are less likely to recognize Harvard’s strength – or, if they come to Harvard, have the chance to interact with a broad array of faculty. While the Harvard-wide Medical Genetics training program is a positive force in this regard and admits as many trainees as they are permitted, this is still a modest number relative to the interest in human genetics - and for other trainees the experience in the genetics of human disease is more variable.

There is little formal relationship between departmental appointment and responsibilities for teaching of human genetics. The first year human genetics course at HMS is taught almost entirely by hospital employees, as are the few courses for graduate students in human and mammalian genetics. Undergraduate teaching at FAS and professional teaching at HSPH has no formal relationship with the course offerings at HMS. The American Board of Medical Genetics training program in clinical and laboratory genetics is supported by the dedicated efforts of a modest number of clinical faculty, and financial support from HPCGG, Childrens and an NIH training grant, but has no formal relationship to the other educational offerings at Harvard.

Translating human genetics discoveries that directly bear on human health

The pace of discovery of genetic variations that influence disease has been meteoric. This new knowledge will broadly impact medicine (e.g., disease prediction and treatment response) and society (e.g., vulnerable populations). We need faculty with diverse expertise including deep understanding of human disease, law and public policy. We need streamlined processes for human genetics research, lowered administrative barriers to collaboration across institutions, and focused efforts to bridge research and the clinic.

Defining goals and monitoring adequacy of shared infrastructure

Infrastructure for human genetics is expensive, and yet confers a major competitive advantage. While the human genetics infrastructure is very good in Boston, we lack a forum in which to debate options, consider priorities, and come together to advocate for future investments or provide feedback. We would benefit from serious study of the competing benefits of fewer centralized cores (in terms of expertise, scale and efficiency) as compared to many local cores (providing convenient access for local investigators).

Developing and supporting the human genetics community

Harvard's human geneticists share many scientific questions, technical needs and organizational challenges. There is great potential in joint research projects spanning our community. Overcoming these needs and capitalizing on opportunities might benefit from greater interaction and coordination as compared to our current ad hoc system.

Possible future models for human genetics at Harvard

The committee debated in meetings and in briefing papers four possible solutions:

- Investment in existing departments and centers, without structural change
- A new Institute or Center for Human Genetics in Longwood
- A new HMS Department of Human Genetics in Longwood
- A new University-wide Committee or Department of Human Genetics

After much deliberation, the majority of our committee favored option four: a new University-wide structure (Committee or Department). This seemed most likely to improve faculty recruitment and retention, education, and integration across the Harvard campuses. This solution seemed most likely to preserve what is good about our current system: its geographic and institutional diversity, its tight connection to other parts of the

system, its innovation and entrepreneurship. All members of our subcommittee felt this was a good solution; one member favored a different solution as is described at the end.

Option 1: Investment in existing departments and centers, without structural change

While continued investment in existing units is necessary and important, we agreed that this alone would do little to address current challenges to faculty recruitment, education, coordinating efforts in translation and infrastructure, and community-building.

Option 2: A new Institute or Center for Human Genetics in Longwood

Harvard has many Centers and Institutes, and in our judgment creating another would not address the challenges we actually face. We questioned the wisdom and viability of gathering human geneticists in one location, extracting them from existing homes and disrupting multidisciplinary interactions essential in our field. We felt that colocalizing some but not all human geneticists at a single location would likely increase, not decrease, institutional competition — and was unlikely to succeed.

Option 3: A new HMS Department of Human Genetics in Longwood

Human genetics is not solely the province of Harvard Medical School, but is of central and growing importance to HSPH and other schools. Creating a department that is solely at HMS would fail to capitalize on the synergies with colleagues in HSPH, FAS, and elsewhere in the university. Moreover, as discussed in greater detail below, creating a new HMS Department of Human Genetics would do damage to existing departments and units, perpetuate the idea that only a quadrangle department can lead a field at Harvard, and fail to engage the multi-disciplinary and multi-institutional nature of the field.

Option 4: A new University-wide Committee or Department of Human Genetics

This final option directly addresses our greatest concerns: faculty recruitment and education, inter-institutional and inter-disciplinary interaction, and community-building.

Faculty development and education: if we can attract and retain the very best people in human genetics (faculty, students, fellows, and staff), and offer the best educational programs, we will ensure a bright future for the field. Recruitment, retention, mentorship and promotion of faculty and students are the responsibility of entities with appointment power, funds for faculty recruitment and promotion, and responsibility for education.

Inter-institutional interaction: human genetics is currently multi-focal, with faculty in Longwood (Quad, HMS and hospitals), at MGH, Harvard Square (FAS and other schools), Kendall Square (Broad Institute of Harvard and MIT), and in the future, possibly Allston. A solution that focuses solely or primarily on a single location will fail to incorporate strengths that exist, nor nurture the interactions essential to our success.

In contrast, a University-wide structure, by design lacking responsibility for a single site, would be charged with building community across and within Harvard's different communities. The leaders of this new entity would have their own opinions and affiliations, but would commit to a University-wide view and responsibility.

Since local community and critical mass are important, we should consider a multi-focal approach in which human geneticists on each campus might be colocated to maximize interactions. The MGH Center for Human Genetic Research offers a successful precedent for this approach, based on the recent move of multiple laboratories into the Simches Research Center adjacent to the Department of Molecular Biology. While in general we do not favor moving human geneticists from one campus to another, human geneticists in a given campus should interact closely without limitation by institutional or departmental affiliation. Closer proximity might foster a sense of shared identity and responsibility for mentorship, without disrupting ties to existing departments. The multiple foci would come together as a University-wide community for the purposes of education, recruitment and community-building.

Inter-disciplinary science: human genetics fundamentally requires deep engagement of basic, clinical and population-based investigators. It is important that in the name of strengthening ties among human geneticists, we not weaken existing connections to other disciplines and communities. We need a solution that embraces the idea that faculty and students from a variety of schools and backgrounds need to be part of our field.

Committee or Department? We considered both Committee and Departmental structures. Our understanding was that a Committee would have (a) tenure track faculty lines and startup funds, (b) authority to mount searches and appoint faculty in partnership with existing departments, (c) responsibility for mentorship and promotion of faculty hired through this mechanism, (d) teaching responsibility across the University, and (e) a forum debating issues important to human genetics at Harvard. We understood that a Committee differed from a University-wide Department in that the latter could search for faculty without a partner department, and administers the laboratory space of its faculty.

Based on this understanding, a majority of our members felt that a Committee would be preferable. By requiring appointments with a home department this mechanism embraces that human genetics is integrated into many parts of the Harvard community. Moreover, having members in many departments would facilitate the mission of broadly enhancing human genetics research, education and community across the University. Our final recommendation, however, will depend on the roles and responsibilities for Committees and Departments as they are defined by HUSEC and the University going forward.

We envision three forms of participation in such a Committee.

Voting Members would be distinguished human geneticists who accept responsibility for: (a) participation in faculty recruitment and promotion, (b) teaching human genetics to students and professionals at all levels, and (c) establishing infrastructure and building community in the field. Rewards would include voting rights in recruitment and promotion, financial contribution to faculty salaries, membership in graduate programs, substantive roles in defining the University's strategy and investments in human genetics, and the satisfaction of creating a world-class human genetics community. Voting Members would be drawn from existing faculty and recruitment of new faculty: both new and old would be treated equally with regard to all rights and responsibilities.

Membership in the Committee would be open to interested faculty, with the goal of maximizing inclusiveness, encouraging communication and building community. For practical reasons, Members would not receive salary support nor share the requirements for teaching and service (though their participation would be welcome). **Affiliate** status would be for interested fellows, students and staff. The Committee would create a web portal, seminar series, postdoctoral and student groups, and other outreach activities.

Leadership and Governance are critically important, and require careful thought. We imagine that the leadership of a University-wide structure would be appointed by the central administration (President and Provost) in consultation with the Dean of HMS and other schools. It is important that the Committee have strong, forward-looking leadership, and the authority to create incentives that maximize participation in teaching and community-building. We imagine that the leader of the new structure will report to a designated Dean, presumably that of HMS. Should the creation of a University-wide structure prove too complex or slow in gestation, there would be value in an HMS-wide solution as an interim solution. But we favor a University-wide model based on the deep interest in the field at HSPH, FAS, HLS, HBS, KSG and throughout the University.

We propose that the leader of a new structure should convene an Executive Committee comprising members of the different components of the University community in human genetics. This Executive Committee will benefit from the perspectives of contributing schools and affiliated institutions, and yet must take as its mandate the greater good of the whole than advocacy for parochial concerns or based on institutional affiliation.

Alternative: a division of HMS Genetics, a new HMS Department of Human Genetics

One member felt that while the Committee structure was acceptable, our diverse set of goals might not best be served through a single mechanism. This individual favored formation of a University-wide organization to coordinate teaching, recruitment and interactions across the University, but in addition a new structure within HMS Genetics with “model system” and “human genetics” divisions. The human genetics division would provide a focal point for the field within HMS, have additional faculty slots to hire human geneticists, and a vice-chair who led its efforts. The two divisions would share in teaching and mentorship, and be led by a single Chair of Genetics.

Conclusion

Human genetics is strong at Harvard; creation of a University-wide Committee has the potential to integrate, expand and embolden this base. A new structure is needed to provide resources to increase and enhance the faculty at Harvard devoted to human genetics, to promote and coordinate human genetics education and community across the University to design, expand, and improve technical platforms, to facilitate translation of genetic discoveries that advance human health. Our challenge is to realize these potential benefits while supporting the tradition of local engagement and entrepreneurial leadership that has served the community well over the years.

Appendix I

Faculty members who participated in the initial discussions initiated by Dean Martin

David Altshuler (HMS, MGH, Broad)
George Church (HMS)
Steve Elledge (HMS, HPCGG)
Jeff Flier (co-chair, HMS, since September, 2007)
Judy Garber (DFCI)
Jim Gusella (HMS, MGH)
Gokhan Hotamisligil (HSPH)
David Hunter (HSPH, BWH)
Raju Kucherlapati (HMS, HPCGG)
Mira Irons (Childrens)
Joseph Martin (co-chair, HMS, until July 2007)
Cynthia Morton (BWH, HPCGG)
Barrett Rollins (DFCI)
Maryellen Ruvolo (FAS)
Christine Seidman (BWH, HMS)
Cliff Tabin (co-chair, HMS)
Chris Walsh (BIDMC, Childrens)