

**UF Genetics Institute Scientific Advisory Board Meeting
February 16-17, 2009**

**SAB Members: Jeff Bennetzen, Rebecca Doerge, Yoram Groner, and Pat Spear
(unable to attend: Ron Davis and Peter Howley)**

The University of Florida's Genetics Institute (UFGI) is comprised of ~200 faculty from numerous Departments and several Colleges. Conceived in 1998, it is centered in the Cancer Genetics Research Complex that it shares with the UF Cancer Center and the ICBR. The mission of the UFGI's SAB is to provide external evaluation and to assist in the identification of limitations to and opportunities for continuing progress in UFGI's service to UF, the state of Florida and the nation. In this third annual meeting of the SAB, we were given the opportunity to assess recent developments in all vital aspects of the UFGI, including infrastructure enhancement, student training, funding status, research progress, and outreach activities. As in our previous visits to the UFGI, the SAB was very impressed by the outstanding operation that Prof. Ken Berns and his colleagues have assembled, and its continued trajectory toward ever-higher levels of excellence. The UFGI provides a unique resource that has accelerated linkages in research and training across the UF campus and beyond. Despite the brevity of its existence, the UFGI has helped individual researchers and the UF achieve international prominence; its continued and increasing value to the University of Florida are both exceptional.

Responses to last year's recommendations:

The SAB was pleased that its recommendations from last year were addressed.

- Improvement in the computational infrastructure of the UFGI since last year has been significant. This improvement complements existing hardware at UF through its focus on large memory computing while addressing the pressing needs of current next-generation sequencing technologies. In its first six months, the new machine (Fisher) served 44 users who submitted 105,203 jobs that totaled 31,610 hours of CPU time. While the Fisher component supplied significant computational relief to the previously stressed infrastructure, the SAB recommends continued monitoring of the UFGI's computation needs in order to keep pace with the ever-growing demands of the latest technologies that are necessary for elite genetic and genomic science.
- The relatively new Genetics Graduate Program is thriving under the leadership of Marta Wayne. The benefit of regular and continued financial support of first year graduate students is evident, as is the support from the faculty who recruit students into their labs.
- While the SAB's request for an overview of the whole institute was addressed from an organization viewpoint (organizational chart and faculty list), we are still anxious to gain a complete/global understanding of the current interdisciplinary projects taking place in the UFGI.
- In its 2008 SAB report, the SAB recommended a regular financial commitment for a pilot grants program specific to the Institute for support of inter-college, interdisciplinary and other collaborative projects. While sustained targeting of a seed grant program to the UFGI has not been implemented, it appears that UFGI staff are making use of UF's university-wide seed money program to which faculty can apply.

- Last year, the SAB expressed support for establishing Systems Biology at UF as a major initiative. This year the SAB learned that Systems Biology at UF is currently on hold, apparently replaced by a focus on Computational Biology.

Computational Biology:

This year, the SAB learned about a faculty-driven recommendation to the University to establish a Computational Biology Center. Computational biology is a necessary and essential component of any serious research institution because it supports both interdisciplinary science and continued training of faculty, staff and students. However, it was unclear how either, or both, the UFGI and the ICBR would integrate with the proposed Computational Biology Center. The SAB is supportive of computational biology at UF and looks forward to hearing more about its continued development next year.

The Interdisciplinary Center for Biotechnology Research (ICBR):

The SAB was highly impressed by the performance and achievements of the ICBR in providing state-of-the-art technical support to the faculty, while maintaining the ability to efficiently respond to the ever-changing genomic technologies life. In so doing, the ICBR has become a driving force behind the leading edge of UF research and development.

Of the various activities of the ICBR (Proteomics, Cellomics, Bioinformatics, Trainings and Genomics), this year's evaluation focused on "next generation DNA sequencing" capabilities, including the integration of both Roche 454 and ABI SOLID sequencing technologies that provide versatility and top performance for rapid whole genome sequencing, as well as ChIP-Seq and RNA-Seq analysis.

The cutting edge competence of ICBR in high throughput deep sequencing and bioinformatics, combined with the UFGI's major interest in translational medicine and cancer genetics, leads the SAB to suggest that the UFGI consider coordinating a joint endeavor by ICBR and the UF cancer center to participate in the new initiative from the International Cancer Genome Consortium (ICGC) [see: <http://www.icgc.org/home>]. The ICGC is an international effort to coordinate a large number of projects aimed at elucidating the genomic changes present in many forms of cancers that contribute to the burden of disease in people throughout the world. The expectations are that the outcome of the research carried out by the members of the ICGC will reveal the genomic alterations in many cancer subtypes and provide valuable information on the methods utilized by ICGC members to produce, analyze, and integrate large genomic datasets related to cancer.

The ICBR deserves to be maintained at the highest level so that it can continue to motivate breakthrough science at UF and the UFGI. This is only possible if the ICBR has the first generation equipment that it has proven so competent to utilize. This exceptional competence is broadly recognized, and thereby explains why the most innovative technology corporations in genomics come to the ICBR at UF to place their most advanced and most transformational equipment. This ICBR also needs a sufficient number of dependably funded staff to make these technologies produce for UF and UFGI researchers.

Additional information requested by the SAB:

Members of the advisory board appreciate being able to focus on selected components of the UFGI on each visit. For the next visit, we recommend that the following be provided, in addition to information on other aspects of the Institute for which advice is sought:

1. More information on collaborations among faculty of the UFGI and on impact of the Institute on the number and quality of these collaborations. For example, over the lifetime of the Institute, what collaborations have developed and have they led to publications and funding?
2. A broader exposure to research at the UFGI, with presentations from scientists in the Institute whom the SAB has not yet encountered.
3. Data on the credentials of graduate students applicants and the students who matriculate. Please include GRE scores and grade point averages of these students. For the students now in the program, their PhD advisors, what are their projects and how close are they to completing their degrees?
4. More information about the actual budget of the UFGI. Where do funds come from, what are the timeframes and hard/soft institutional commitments to the UFGI, and how are these funds dispersed?

General comments:

The SAB was impressed by all of the presentations that were made at this annual meeting. The discoveries outlined in brief seminars by Drs. Bailey, Gravlee, Hauswirth and Mulligan were landmark accomplishments that rank in the highest echelons of life science research. Any faculty in any research institution in the world would be proud to feature such contributions. The innovative and comprehensive approach to bringing genomics into the undergraduate curriculum presented by Dr. Triplett was exceptional both in its creativity and its potential to rectify deficiencies in the US higher education strategy that have been identified in studies by NSF and other organizations. Dr. Marta Wayne's energetic and forthright stewardship of the UFGI graduate program continues to be a highlight of the Institute. The graduate program is headed in the right direction, at a brisk pace, with excellent results in student training and integration into the UF research environment. The Annual UFGI Symposium has been a huge success, bringing together colleagues across UF and increasing the visibility of UF and the UFGI in the international science community. Discussions with Drs. Frazier, Good, Khargonekar, McLellan, Richardson, Jaishankar and Phillips all indicated a tremendous appreciation at UF of the unique value of the UFGI. Even in these difficult fiscal times, these leaders understood that the UFGI provides an unmatched resource that empowers research across the entire UF campus. Investments and capacity building in the UFGI and the ICBR have been repaid many times over, and need to continue if the UF wishes to retain its prominence in life sciences research.

Recommendations

The UFGI is in excellent shape at this time. Moreover, the UFGI has an institutional vision and organizational structure that are prepared for whatever future the UF environment will provide. However, some vital issues need to be resolved in order to maintain UFGI excellence. In addition, opportunities were identified by the UF faculty and the SAB that can take the UFGI to a higher level and thereby dramatically enhance the research and training environment at UF.

- **Creation of an ensured, flexible and transparent funding model for the UFGI.**

Although the SAB is not fully cognizant of the funding status of the UFGI, we have the general feeling that it is run on a shoestring and by funds that are not guaranteed from year to year. If some indirect costs were contributed to the UFGI, a logical outcome of the provision of facilities and students by the Institute, then this could increase buy-in to the UFGI program, provide stability for staff support, and create a bridge/seed fund for future needs of UFGI faculty and students.

- **Stable budgetary support for key computational biology staff, and greater staff depth.**

The tremendous advances in computational biology capacity and integration made in the last year at the UFGI have already brought science at the UF to a new level. Highly qualified support personnel are now in place to facilitate this operation, but the staffing is minimal and maintained on soft funds. Because the illness or departure of a single key staff member could shut down much of the computational capacity at UFGI, there is a need for additional staff that would provide continuous and seamless support.

- **Acquisition and innovation with the most advanced genome sequencing platforms.**

The ICBR needs to be kept at the forefront of life sciences technology. This is particularly pertinent in the area of next generation DNA sequencing. This field is changing so rapidly, with unequaled discovery potential in a technology that is central to all of the life sciences, that wholly new visions of what can be accomplished are almost daily occurrences. The ICBR, due to its history as a “first implementer” and innovator, is recognized worldwide as a place where new genomic technologies will be mobilized. Hence, the ICBR provides all UF researchers with a tremendous advantage in employing new approaches to genome characterization before other institutions are even aware that these approaches exist. This premiere status must be maintained.

- **Initiate a fully open (external and internal) search for a new UFGI Director.**

The contributions of Prof. Ken Berns to the establishment, operation and growth of the UFGI are impossible to overstate. His vision and leadership have been at the core of UFGI’s success, and this high level of contribution has not diminished. However, Dr. Berns has stated that he will be retiring from the directorship of the UFGI within the next 16 to 20 months. Hence, it is urgent that the search for a new Director commence as soon as possible. The position of Director is essential to the UFGI. UF should search for a researcher with exemplary status, vision and energy to fill this role.

- **Application for a training grant to support the UFGI graduate program.**

The UFGI graduate program has been a tremendous success so far. It could use additional outreach efforts to increase the applicant pool and also needs to resolve issues regarding the inconsistent availability of an appropriate statistics course. The Director of the

Graduate Program, Dr. Wayne, deserves commendation. However, her term ends soon, so this leadership issue needs to be resolved. Support, in the form of laboratory assistance or teaching relief, for instance, is essential to help the next Director devote the necessary time to the graduate program. In this regard, because the UFGI graduate program now has a track record, an exceptional cohort of training faculty and high quality students, it is time to apply for external support for the graduate program.

- **Investigation of the possible advantages and costs of a Computational Biology program at UF.**

Continued progress in the conceptualization and planning of a Computational Biology Program is important. This CBP could be an effective strategy to link the distributed and core computational capacities of the university, and to promote synergy in the multi-disciplinary pursuit of key questions in medicine, agriculture and the natural sciences.

- **Establishment of a seed grant program for the UFGI.**

The value of seed grants is exceptional, especially if targeted at a productive program that has numerous young scientists with outstanding potential. The UFGI is replete with these developing scientists, and so a seed grant program available specifically to the UFGI is warranted. These grants would be most valuable if they required an interdisciplinary UFGI link. The value of such a program, within the UFGI, should be tabulated and used as an evaluation tool for calculating UF cost-to-payoff for such a commitment to the UFGI.

UF Genetics Institute Scientific Advisory Board Meeting February 21-22, 2008

SAB Members: Jeffrey Bennetzen, Yoram Groner, Pat Spear, Eric Olson, Rebecca Doerge, Ron Davis and Peter Howley

The UF Genetics Institute occupies part of a state of the art building shared with the UF Cancer Center and the ICBR. The UFGI is also a virtual institute with members located throughout different colleges in the university. This was the second meeting of the SAB and we feel that Ken Berns continues to do an outstanding job of building and organizing this important interdisciplinary initiative for the university.

This year the SAB heard about the bioinformatics group, the statistical genomics group, the graduate program and the new initiative in Systems Biology. This complemented the major areas of gene therapy and plant genetics that we heard about last year. At next year's SAB meeting it would be good for an overview of the whole institute to be provided along with a complete list of its faculty and their programmatic areas.

The two major areas of emphasis in the UFGI (gene therapy and genetics/genomics) present problems with regard to development of more robust infrastructure in the future. The two areas require different types of support and prioritization.

Although investments made by the university and the state have been substantial, the UFGI is in desperate need of ongoing annual support to sustain and enhance this important trans-university effort. There is a need for a more robust ongoing annual budget to maintain the scientific infrastructure if the long term potential of this initiative is to be achieved. Major areas require regular financial support and continued attention:

- the computing infrastructure,
- the new Genetics and Genomics graduate program
- pilot grants program specifically within the Institute to foster inter-college and other collaborative projects.

Ongoing investments in these areas are necessary to continue the natural progression of the UFGI.

Systems Biology:

The SAB was pleased to see that the incipient Systems Biology program at the University of Florida has taken significant strides to extend and integrate its cross-campus interactions. The fact that an exciting Systems Biology approach to the study of carnatine metabolism and ketogenic therapy was initiated through contacts made at the last SAB meeting was particularly nice to hear. Although the definition of Systems Biology remains fluid, the ongoing efforts at UF to link engineering, computer sciences, statistics and the life sciences into a comprehensive and quantitative analysis of biological systems is wholly appropriate. These linking efforts need to be continued at UF, and all evidence presented to the SAB indicates that this will occur with major contributions from UFGI faculty.

There is great enthusiasm for Systems Biology at UF, including in the UFGI, particularly among the junior faculty. Excitement about this discipline is also clear at the national level, as shown by funding agency directives and the clamor by students for courses and degrees in this area. It is highly appropriate for a Systems Biology community to be grown at UFGI, as this represents one of those rare opportunities where a world-class operation can be built without a huge demand for new resources. As such, a Systems Biology emphasis would pull UF towards a higher level of recognized scientific excellence.

A visionary leader is needed to bring Systems Biology to this level of international prominence. Although it would be fully justified for this senior or mid-level individual to be a member of the UFGI faculty, given the central role of genetics and genomics in Systems Biology, the appropriate leader could also be drawn from other disciplines like statistical genomics or biomedical engineering. The few productive senior scientists with Systems Biology expertise are in high demand and it is not clear that UF could recruit such an individual without very large resource commitments. It is more likely that a visionary scientist with a Systems Biology interest but no major previous expertise could be recruited, from either an internal or external source. Most, perhaps all, of the life sciences will eventually become the target of Systems Biology, so any biologist with vision would be likely to fit this bill.

Immediate needs to bring Systems Biology into the mainstream here at UF involve the possible targeting of seed grants for this subject and support (e.g., teaching load reduction) for the junior faculty who have currently been leading the Systems Biology charge at UF. They are clearly willing and able to move this activity forward at UF right now. Systems Biology should be promoted as a target point for the UF and UFGI Development Officers (“Systems Biology will explain and allow the understanding of all biological systems, and in the future will be the foundation for all medical solutions, agricultural improvements, and environmental preservation/reinvigoration.”) This selling point sounds grandiose, which it is, but is it also true at its core).

Establishing contacts on campus to communicate the state-wide and university-wide value are appropriate. The directors of the UFGI and the new Emerging Pathogens program would be particularly important individuals to provide their insight and assistance.

Graduate Program:

The graduate program is off to a solid start with nine students having joined the program in the past two years. The students are enthusiastic and generally happy. There is a need to continue to recruit additional students, especially U.S. students, since nearly all the students are foreign. At present, there has not been advertising for the graduate program. Marta Wayne is doing an outstanding job leading the graduate program. However, as the program grows, it will be essential to have additional advisors for the students. This is a particularly important issue in the first year when most students arrive from overseas and

need help establishing themselves. A big brother/sister program in which senior students take responsibility for helping new students get situated in Gainesville would be very helpful. The students noted a desire for their graduate program to have more of a recognized identity within the University. This will come, of course, with greater maturity of the program but perhaps some efforts could be made to accelerate this development. Efforts to attract minority students to the program should also continue to be encouraged.

Bioinformatics:

The UFGI bioinformatics group continues to make excellent strides in establishing and maintaining collaborative research projects that involve a number of scientists and students across campus. Professors McIntyre and Triplett provided three excellent examples (drosophila, maize, pine) of interdisciplinary collaborations among experimentalists, statisticians, breeders both at the University of Florida and at other universities. As part of each of these collaborations a great deal of data are being generated. It is anticipated that the level, size and complexity of these data will continue to grow as the technologies improve and evolve. Toward this end the UFGI is not well positioned to maintain or meet the growing computational needs of bioinformatics. This weakness not only challenges the foundation of the current bioinformatics initiative, it undermines the commitment of the university thus far in recruiting young and mid-career faculty. Without the appropriate computational infrastructure to support bioinformatics, UFGI runs the risk of not keeping up with science and technology, and not retaining or recruiting faculty and graduate students. The current bioinformatics faculty members are working hard to maintain their research programs and grow the graduate program while dealing with the lack of computational infrastructure and support. With no computer system administrator, no interface to the existing computational system, and no budget to remedy these issues, the faculty members are stretched to write grants and attempt to fix the computation problems themselves. The committee strongly recommends that the university provide a computational infrastructure run by a qualified hard money system administrator to support the growing needs of the UFGI which is currently significantly underpowered and understaffed.

Examples bioinformatics institutes with varying levels of monetary support when setting up their bioinformatics computational infrastructure to support bioinformatics, genomics, systems biology, etc. include: The Broad Institute; The Institute for Systems Biology Virginia Bioinformatics Institute; and The National Center for Genome Resources to name only a few. The organizational structure of any bioinformatics facility includes data generation, data organization, and data analysis. A core computational infrastructure run by qualified staff dedicated to these three components support the wet-lab facilities, the databases require to stored data in an organized manner, and the data analysis components that help to answer the biological question.

Statistical Genomics:

The statistical genomics group at the UFGI is fully integrated and thriving under the leadership of Professor Casella. The advisory board heard about a successful weekly discussion group, established research collaborations, the graduate program, and shared advising of students. Professors Casella and Davis, themselves, present an example of a successful interdisciplinary collaboration that is well funded by federal money that continues to be enabled by the UFGI. It is evident from what the advisory board heard that the UFGI is bringing people together and good things are happening as a result. However, the lack of a computational core infrastructure is a current limitation to the needs of the statistical genomics people in the UFGI. High power computing, long range data storage and qualified staff to maintain the system need to be made a priority.

Succession:

One important issue that needs to be considered by the leadership at UF is that of succession. Ken Berns indicated that he plans to step down as the director of the UFGI within 2 to 3 years, and a process should be established soon to identify the next director. The SAB feels this could be an extraordinary opportunity to bring additional genetics/genomics leadership to UF. Looking outside the UF community for such a leader, as well as inside, would be advisable.

UF Genetics Institute Scientific Advisory Board Meeting
February 19-20, 2007

SAB members: Jeffrey Bennetzen, Yoram Groner and Peter Howley

The UF Genetics Institute is in its inaugural year located in a newly constructed building that it shares with the UF Cancer Center. Ken Berns has done an extraordinary job in organizing and recruiting faculty to this new cross-school interdisciplinary initiative at UF. We were impressed by the commitment and high level of interaction among the program leaders and scientists whom we met during the course of our day and a half visit to the UGFI. The new research building is an attractive state of the art facility that also houses the high end Interdisciplinary Center for Technology Research core facilities. The investment that UF has made in the building and setting up of the laboratories that comprise this new interdisciplinary research initiative has been significant, however the UFGI will also need an ongoing annual budget from the UF for recurring expenses to maintain the scientific infrastructure that has been put in place if the long term potential of this initiative is to be achieved. Long term stability for this support could be achieved if this were to be provided as a state line budget item.

The UFGI is an important interdisciplinary initiative for the university and has the potential to help in lowering the walls between departments and schools within the university. To that end, we would recommend that for any new faculty positions, it would be appropriate that all hires be justified for their value to the University, not just to satisfy the needs of any single Department or Program.

We heard from Nick Muzycka, Terry Flott and Arun Srivastava about the Gene Therapy program at UFGI that is currently under the direction of Barry Byrne. Both Nick and Arun are long tem associates of Ken Berns and have each been major leaders in the development of the parvoviruses as effective gene therapy vectors. This group is one of the leading gene therapy groups in the United States and has been enhanced by recent faculty hires. Although these new faculty were hired on the basis of open national searches, it appears that many are trainees of the senior members of the group. While in the short run the hiring of previous trainees may enhance collaboration and the ability to fund program grants, in the long run it will be important to expand the hiring of new faculty to individuals that have been trained elsewhere to avoid becoming too inbred. Although there has been some use of lentiviruses and non-viral vector systems, the major strength of the group has been the optimization and the utilization of parvovirus vectors. There is a major commitment to the basic molecular biology of this group of viruses with the goal of furthering the utility and development of parvovirus vectors in human gene therapy. The current focus is on the large family of AAV types and B19 as vectors. A broad focus of potential human diseases potentially amenable to gene therapy was presented and for many of these diseases, animal models are available. Additional opportunities for this group would be in the use of gene therapy in cancer. To do so would require coordination with translational scientists at the cancer center. One obvious area in which to expand would be in the area of mouse models for cancer. This gene therapy group could also be enhanced by extension to additional viral vector systems, such as the adenoviruses (particularly if they were to extend into the area of cancer therapy).

The plant genome group has a major strength in maize genetics, and productive researchers in several other plant genetics and genomics disciplines. Intra-campus collaborations appear to be

strong, and many labs are involved in productive inter-institutional collaborations. It appears that the bioinformatics capacities at UF are not sufficiently linked with this group, and may require additional faculty lines and/or more motivation for this interaction. Translational capacities are clearly insufficient, requiring the addition of faculty focused on modern crop improvement at such levels as marker-assisted selection or transgenic development. The number of faculty devoted to cell biology, developmental biology and model systems (e.g., Arabidopsis) also appear to be insufficient to provide a universally excellent plant science capacity.

Engineering at UF has made a major commitment to the life sciences, and is desirable of additional links with UFGI. A logical foundation for further interaction between engineering and UFGI is in the general area of Systems Biology.

The ICBR is a great strength at UF, and a tremendous resource for the state of Florida. The ICBR appears to be under skilled management. Current efforts to establish an advisory committee are highly praiseworthy, and the mission of this committee should include regular evaluations of the individual cores within the ICBR. If additional service bioinformatics is needed, the ICBR would be a good place to house it.

The UFGI Bioinformatic group consists of 11 researchers that study a broad spectrum of bioinformatic related topics including system biology, computer science and Math/Statistics. The group defined its mission as conducting innovative research in functional genomics and system biology. These include generation of databases and tools for analysis, and development of new algorithm and methodology to solve system biology problems. The UFGI group has extended collaborations with investigators in different colleges such as Medicine, IFAS and Museum of Natural History. The group participates in the graduate and postdoctoral training programs. The committee was impressed by the high level of the research projects presented, all of which investigate mainstream issues in bioinformatics particularly in system biology. The committee thought that combining “wet” and “dry” activities within the same research group (that is being done by several UFGI BioInfo investigators) has a potential for highly innovative and productive research. The committee however expressed concerns over the apparent lack of long-range collaborative projects between the BioInfo group and other UFGI groups, and recommended establishing mechanisms to foster stronger collaborations within the UFGI for members of the BioInfo group.

The UFGI graduate program is a vital addition to UF. The program is well-conceived and off to a good start. Given the proper attention and emphasis it should contribute immensely to the coherent development of the various elements comprising the UFGI, and enhance the visibility of the UFGI throughout the university. We met with the first group of four UFGI students who were very positive about the program and the rotation system, which is an excellent component that should help build interactions across the program. Additional efforts to build cohesion among the graduate students are planned, and these need to be vigorously pursued. The University must make a recurring, long-term commitment to graduate student support, and the application for training grants to support this new graduate training area. A key to the success of any graduate program is intense recruitment efforts, and the UFGI needs to be both visible and effective at emphasizing the unique strengths of its programs. It is recommended that it emphasize its systems approaches and strengths in graduate training to take advantage of the keen interest now in Systems Biology programs by graduate school applicants.

