**EIPOD Reference**

1. Please comment on:

* The knowledge of the applicant with regard to his/her field of research.
* The motivation and work ethic of the applicant.
* The capability for practical laboratory work, or technical equivalents such as programming.

If possible, please also try to specify the kinds of techniques where you think the applicant is strong. (maximum 2000 characters)

Aaron Brooks is a talented and creative young scientist with exceptional skills in both bioinformatics and experimental molecular biology.

Aaron joined my lab in April 2015. His current project investigates the effects of genetic variation at several biological scales. Specifically, he is dissecting the consequences of genetic variation in a segregating yeast population by combining multiple omic measurements, including quantification of the genome, transcriptome, proteome and metabolome. Integration of these high-throughput data sets remains a significant challenge in the field, in part because of the diversity of expertise required to produce, analyze, and interpret these many facets simultaneously. I brought Aaron on the team because he has the background to do exactly this. This project will also serve as important stepping-stone for his more ambitious project as an EIPOD fellow. Aaron has proposed an EIPOD project that is an exciting new direction building from his existing project but at an even more impressive scale.

Aaron has the background, technical expertise, and work ethic to guide a complex project to its completion. His deep biological knowledge is complemented by technical proficiency and creativity. Aaron can perform computation as well as design and perform experiments – a powerful combination for a 21st century biologist. This is why I selected Aaron for his original project and why he will thrive as an EIPOD fellow, despite the immense challenge of the project. He has previously developed sophisticated computational pipelines, managed large bioinformatic databases, created web applications, and performed and analyzed high-throughput experiments. After only a few months in my lab he has already established a new computational method for QTL detection and built an interactive web application.

I am convinced that Aaron has the required skills, ambition and motivation to be highly successful in his EIPOD research.

1. Give your opinion of the applicant considering the following criteria: theoretical knowledge, interaction with colleagues, adaptability/flexibility, technical proficiency, motivation/commitment, creativity/originality, independence, communication skills. (maximum 3500 characters)

I am highly impressed by Aaron’s advanced knowledge in systems biology. The skills he gained during his PhD have already been applied to projects in my lab and will open new and exciting scientific avenues in the future.

Theoretical knowledge: Aaron has detailed theoretical knowledge of biology, computation, and complex systems. He has even participated in the Santa Fe Institute’s prestigious Complex Systems Summer School

Interaction with colleagues: Aaron is a friendly person. He is respected by his co-workers and has established himself as a senior member of my team. He proactively organized a computational working group to discuss consolidation and management of laboratory data and pipelines, as well as provide advice for computational challenges in the lab. Aaron has orchestrated his EIPOD project to synergize with the research activities of other senior members of my group.

Adaptability: Aaron is highly adaptable and flexible. Aaron’s transition into the lab, for example, was seamless. Despite coming to the lab to work on a project that is quite different from his PhD project, Aaron hit the ground running. His adaptability is also evidenced by his decision to join my lab at EMBL in Germany rather than my lab at Stanford in his home country, which would have been an easier transition for him.

Technical proficiency: Aaron has technical expertise in bioinformatics. He is fluent is several programming languages, including R, Python, JavaScript, and SQL. Aaron has built and maintained algorithms, pipelines, large databases, and web applications. He also has technical proficiency in experimental biology, including molecular biology methods, microarray- and sequencing-based transcriptomics, and fluorescence-based methods (microscopy and cell sorting).

Motivation: Aaron is a highly motivated and committed scientist. Even before his official start date, he was hard at work on a pending grant application. Aaron has been eager to take on additional responsibilities in my lab, including mentoring several interns. He has followed through on all of the commitments he has made.

Creativity: Likely due to his diverse background, I’ve noticed that Aaron tends to think in “out-of-the-box” ways about biological problems. He is a well read and forward-looking. He talks often about new technologies and approaches, even if these come from other fields. For example, in his PhD he adapted algorithms typically applied to social networks to make sense of biological networks.

Independence: Aaron is highly independent. Since joining the lab, he has managed several collaborations and projects with minimal oversight. For his EIPOD application he has independently crafted a project that drives our existing research forward in an exciting new direction while still leveraging the ongoing work of his colleagues.

Communication skills: Aaron is able to communicate effectively in a variety of formats. In the few months since joining EMBL he has provided two public lectures: an invited talk for the centre for biological network analysis (CBNA) and a presentation to the multiomics journal club organized by Judith Zaugg. Aaron is active on social media (Twitter), maintains a website to communicate his research, and has been involved in several public outreach campaigns, including design of an outreach activity for a national science fair in the US before joining my lab.

**HFSP Reference**

1. Research experience

2013–pres. Professor of Genetics, Stanford University.

2013–pres. Co-Director, Stanford Genome Technology Center, Stanford University.

2013–pres. Associate Head of Unit and Senior Scientist, European Molecular Biology Laboratory.

2009–2013 Joint Head of Unit and Senior Scientist, European Molecular Biology Laboratory.

2003–2013 Group Leader (Visiting), Stanford Genome Technology Center, Stanford University.

2003-2009 Group Leader, European Molecular Biology Laboratory

2002–2003 Postdoctoral Fellow, Stanford University School of Medicine, Department of Biochemistry and Stanford Genome Technology Center.

1997–2001 Howard Hughes Predoctoral Fellow, Stanford University School of

Medicine, Department of Genetics.

1. Publication List  
   Please list up to 10 publications in areas closest to the applicant’s proposed research, including title, journal, author(s) and year. Number your publications starting from “1”.
   1. Steinmetz, L.M., Scharfe, C., Deutschbauer, A.M., Mokranjac, D., Herman, Z. S., Jones, T., Chu, A.M., Giaever, G., Prokisch, H., Oefner, P.J. & Davis, R.W. Systematic screen for human disease genes in yeast. Nature Genet. (2002).
   2. Steinmetz, L.M., Sinha, H., Richards, D.R., Spiegelman, J.I., Oefner, P.J., McCusker, J.H. & Davis, R.W. Dissecting the architecture of a quantitative trait locus in yeast. Nature (2002).
   3. Mancera, E., Bourgon, R., Brozzi, A., Huber, W. & Steinmetz, L.M. High-resolution mapping of meiotic crossovers and noncrossovers in yeast. Nature (2008)
   4. Blandin, S.A., Wang-Sattler, R., Lamacchia, M., Gagneur, J., Lycett, G., Ning, Y., Levashina, E.A. & Steinmetz, L.M. Dissecting the genetic basis of resistance to malaria parasites in Anopheles gambiae. Science (2009), PMCID: PMC2959166
   5. Wilkening, S., Pelechano, V., Järvelin, A., Tekkedil, M.M., Anders, S., Benes, V. & Steinmetz, L.M. An efficient method for genome-wide polyadenylation site mapping and RNA quantification. Nucleic Acids Res. (2013).
   6. Pelechano, V., Wei, W. & Steinmetz, L.M. Extensive transcriptional heterogeneity revealed by isoform profiling. Nature (2013).
   7. Gagneur, J., Stegle, O., Zhu, C., Jakob, J., Tekkedil, M.M., Aiyar, R.S., Schuon, A.K., Pe’er, D. & Steinmetz, L.M. Genotype-environment interactions reveal causal pathways that mediate genetic effects on phenotype. PLoS Genetics (2013)
   8. Wilkening, S., Lin, G., Fritsch, E.S., Tekkedil, M.M., Anders, S., Kuehn, R., Nguyen, M., Aiyar, R.S., Proctor, M., Sakhanenko, N.A., Galas, D.J., Gagneur, J., Deutschbauer, A. & Steinmetz, L.M. An Evaluation of High-Throughput Approaches to QTL Mapping in Saccharomyces cerevisiae. Genetics (2014).
   9. Fritsch, E.S., Chabbert, C.D., Klaus, B. & Steinmetz, L.M. A genome-wide map of mitochondrial DNA recombination in yeast. Genetics (2014).
   10. Aiyar, R., Bohnert, M., Duvezin-Caubet, S., Voisset, C., Gagneur, J., Fritsch, E., Couplan, E., von der Malsburg, K., Funaya, C., Soubigou, F., Courtin, F., Suresh, S., Kucharczyk, R., Evrard, J., Antony, C., St.Onge, R.P., Blondel, M., di Rago, J.-P., van der Laan, M. & Steinmetz, L.M. Mitochondrial protein sorting as a therapeutic target for ATP synthase disorders. Nature Commun. (2014).
2. Reference  
   In this section you will be required to provide a letter of recommendation assessing the applicant’s qualifications and suitability to perform the proposed research. You will first be asked to confirm that you are supporting only one applicant and that you have seen and approved the research plan. You will also be asked if you have interviewed the applicant and to indicate how many Postdocs, Ph.D. students and technicians are currently in your laboratory. In 2-3 pages you should endeavor to convince the review committee that the proposed research project is novel, high impact and provides an excellent opportunity for the applicant to expand their expertise to achieve their career goals.

The evaluation criteria to be addressed are:

Originality and contribution:

* Novelty of the proposed research project; the applicant’s intellectual contribution in developing the proposal; expected impact of the proposed work; potential of the research to move the field forward.

Learning potential and knowledge exchange:

* The learning potential for the applicant through exposure to new techniques and literature; the knowledge/techniques the applicant will bring to the lab (particularly important for Cross-Disciplinary Fellowship applicants); unique synergy that will be achieved through hosting the fellow in the proposed laboratory.

Career development:

* Alignment of what will be learned during the fellowship with the knowledge needed by the applicant to pursue their career goals; possibility of the proposed work to build the applicant’s international network of collaborators; the suitability of the proposed host laboratory environment to nurture the applicant’s career goals

**Reference for Aaron Brooks**

Dear Evaluating Committee,

I would like to provide the strongest recommendation for my postdoctoral student, Dr. Aaron Brooks, to be selected for the Human Frontier Science Program postdoctoral fellowship program. Aaron Brooks is a talented and creative young scientist with exceptional skills in both bioinformatics and experimental molecular biology. I am convinced that Aaron has the required skills, ambition and motivation to be highly successful in his research as an HFSP fellow.

I am an expert in genomics research and technology development with many years of experience managing interdisciplinary projects and international collaborations. I am Professor of Genetics at Stanford University and Co-Director of the Stanford Genome Technology Center. In addition, I have been leading a research group at the European Molecular Biology Laboratory (EMBL) and served as founding chairman of its Genome Biology Unit. My laboratory develops and applies cutting-edge technologies to investigate the genetic basis of diseases, with the ultimate goal of developing personalized, preventative medicine. We designed the first tiling microarray for yeast, which was a technological breakthrough that changed the view of how genomes are expressed. We also performed the first high-resolution, genome-wide map of yeast meiotic recombination outcomes, which has been described as a landmark in the field. These seminal approaches have become gold standard in transcriptomics and our technologies are now widely applied by others.

Aaron started in my lab in April 2015. His joined my lab to investigate the effects of genetic variation at several biological scales. Specifically, he aims to dissect the consequences of genetic variation in a segregating yeast population by combining multiple omic measurements, including quantification of the genome, transcriptome, proteome and metabolome. Integration of these high-throughput data sets remains a significant challenge in the field, in part because of the diversity of expertise required to produce, analyze, and interpret these many facets simultaneously. I hired Aaron because he has the background to do exactly this. He is applying to the HFSP program with an ambitious and exciting proposal wherein he will take this project in a significantly new direction, expanding his technical expertise and establishing international collaborations that will help launch an independent research career.

From my working experience with Aaron, I have learned that he has the background, technical expertise, and work ethic to guide complex projects to their completion. His deep biological knowledge is complemented by technical proficiency and creativity. Aaron can perform computation as well as design and perform experiments – a powerful combination for a 21st century biologist. This is a major reason I selected Aaron from among many talented applicants and why he will thrive as an HFSP fellow, despite the immense challenge of the project he has proposed. He has previously developed sophisticated computational pipelines, managed large bioinformatic databases, created web applications, and performed as well as analyzed high-throughput experiments. He is fluent is several programming languages, including R, Python, JavaScript, and SQL and has technical proficiency in experimental biology, including molecular biology methods, microarray- and sequencing-based transcriptomics, and fluorescence-based methods (microscopy and cell sorting). After only a few months in my lab he has already established a new computational method for QTL detection and built an interactive web application, which he is preparing for publication.

Aaron also collaborates well, which will be an important component for success in his HFSP project. He is respected by his co-workers and has established himself as a senior member of my team. Aaron, for example, proactively organized a computational working group to discuss consolidation and management of laboratory data and pipelines, as well as provide advice for computational challenges in the lab. With respect to the HFSP proposal itself, Aaron has carefully crafted it to synergize with ongoing research activities of other senior members of my group, as well as play to the strengths of our international collaborators.

Aaron has proposed an ambitious project to (1) decipher how genetic-factors contribute to wellness, (2) predict wellness from a combination of genotype and molecular information and (3) understand how the environment modulates these genetic effects. Starting from quantitative measures of “wellness” in a segregating, budding yeast population, Aaron will discover molecular hallmarks that are indicative of health and its decline and measure how these effects depend on the environment.

Specifically, Aaron will use aging in yeast as a proxy for wellness. Yeast has been used previously as a model system to study conserved molecular processes involved of aging, where a yeast’s maximum “age” can be quantified as the number of budding events a mother cell undergoes before it can no longer produce buds. Aaron will measure how the ageing phenotype varies across a genetically diverse population of hundreds of genotyped yeast segregants. These strains were constructed in my lab as a cross between a laboratory strain of *S. cerevisiae*, S288c,and a pathogenic strain isolated from the lungs of an AIDS patient, YJM789. After identifying genetic factors underlying a predisposition or recalcitrance to aging, Aaron will investigate how these genetic factors relate to molecular hallmarks that are indicative of the ageing process itself. These hallmarks will be identified by measuring changes at multiple molecular levels (epigenome, transcriptome, proteome, metabolome) in a subset of the segregants at several stages of the aging process using a technique that is currently being developed by another senior researcher in my lab to isolate individuals of a specific age. Finally, Aaron will determine the environmental-specificity of the genetic effects and molecular hallmarks by leveraging the documented heat tolerance of YJM789 to characterize how genetic influences and molecular hallmarks change at elevated growth temperatures.

What excites me most about Aaron’s project is its immediate relevance to personalized health in humans. Several scientific projects and now private companies have initiated projects to monitor and manage wellness. These efforts typically combine DNA sequencing with real-time molecular profiling (blood biomarkers, microbiome composition, etc) and coaching to improve health. While deciphering the genetic contribution to wellness in a human population will present new challenges, Aaron’s methods will have immediate application with respect to how the molecular profiles should be integrated and interpreted by these companies. In fact, as a final aim of Aaron’s project we hope to partner with a new wellness company called Arivale (a company started by the head of Aaron’s previous Institute and my collaborator, Lee Hood) to adapt Aaron’s computational approaches for identification of molecular fingerprints predictive of human wellness. In addition to its utility for real-time wellness monitoring, the novelty of the integrative, multi-omic computational methods and cutting-edge experimental techniques used to isolate and measure multiple molecular profiles in yeast of a defined age will ensure that Aaron’s project is impactful. I have no doubt that the tools developed by this project will be applied broadly to advance research in the yeast community.

This project and the HFSP fellowship are an excellent opportunity for Aaron to gain valuable research expertise and establish international research collaborations that will help him become a leader in the field. Aaron’s career has already undergone a major transition. Immediately prior to his PhD Aaron started gaining expertise in the computational sciences, having been trained as a wet-lab experimental biologist. This project will represent a second major transition in his career – albeit a transition in scale rather than type. The project Aaron has proposed is extraordinarily ambitious in scale. It will require careful oversight and planning. For this Aaron has established regular milestones to keep the project on track. The project will also require extensive collaboration. We have established collaborating partners throughout the world (e.g., EMBL Heidelberg, EMBL-EBI, Stanford, University of Luxembourg, Institute for Systems Biology) who will contribute their expertise in data collection and analysis. Aaron is actively working with several of these groups already to develop data collection and analysis pipelines for transcriptomic, metabolomic and proteomic measurements in yeast, which will be used in this project. Working with these groups will allow Aaron to expand his technical expertise and establish valuable research partnerships that he will be able to take with him in his independent career. Finally, the project will require efforts from a number of researchers, including technicians, students, and other senior researchers. Because Aaron will be at the center of this project, he will gain important managerial experience and training that will be beneficial to him as he develops his own lab.

Aaron will be successful in his proposed HFSP project because he is talented, careful, independent, collaborative and hard working. He will be supported by extensive resources in my lab and in the labs of my collaborators across the world. Aaron has cleverly designed the study to bring together multiple pre-existing resources in my lab. Since Aaron is already managing an international collaboration with minimal oversight, I expect that will be able to effectively navigate and leverage these resources as well.

I fully endorse Aaron and his application for your fellowship given both his personal merits as well the scientific significance of the project itself. HFSP funding will help Aaron establish methodologies, additional expertise, and – importantly – international collaborations that will propel him forward towards a successful future career.

Please do not hesitate to contact me if you require further information.

Sincerely,

Lars Steinmetz