



DEPARTMENT OF BIOLOGY

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To whom it may concern:

I write this letter *with the strongest possible support* of Dr. Rafael Guerrero's application for a faculty position at Florida State University. Rafael and I have been working together for five years now, giving me time to observe his obvious abilities as an outstanding scientist and the maturity we expect to see in junior faculty.

I can attest to the fact that Rafael is a creative, original researcher who is successfully applying his excellent training in theoretical population genetics to an assortment of problems in evolutionary and computational genomics. And I believe that this combination is the future of evolutionary biology—mathematically inclined biologists with excellent quantitative skills who migrate towards asking the big questions that can be answered with a combination of evolutionary theory and large datasets. Rafael is clearly the type of scientist who knows what the big questions are, and I have seen how quickly he has picked up new skills that will enable him to carry out fruitful research on these questions for the foreseeable future.

Rafael's dissertation work clearly demonstrates his ability to do original theoretical research in evolutionary genetics. The two major topics this work covered are the dynamics of chromosomal inversions and the dynamics of sex chromosomes. The work on inversions provided a novel framework for understanding why these are often maintained as polymorphisms within species, and specifically enabled us to understand where the important mutation(s) underlying differences between arrangements reside. His work on sex chromosomes is related in the sense that these also represent a recombination-limited system of alternative chromosomes, and that the goal of much of the work was to identify the location of sexually antagonistic polymorphisms distinguishing newly evolved X and Y chromosomes. His additional participation in a large group of researchers involved in thinking about the evolution of sex chromosomes (the "Tree of Sex" catalysis meeting) has meant that he has also been exposed to and has published on wider issues involving sex chromosomes.

Rafael has continued to work on both of these topics while in my lab, in addition to extending his research into new areas. Rafael has continued his work on sex chromosomes by initiating the

study of a new system of closely related species, *Solanum polygamum* and *S. appendiculatum* (both are relatives of domesticated tomato). These species both have newly evolved sex chromosomes, and Rafael has already sequenced the genome of *S. polygamum* with the aim of applying the theoretical framework he developed during his Ph.D. to identify the mutations driving the initial differentiation between sex chromosomes. This system has a lot of potential, and in order to do all of this work Rafael has had to master many areas of genomics and bioinformatics that were new to him, using a combination of Illumina and PacBio sequencing. I have been very impressed with his ability to quickly pick up these new skills and to apply them in innovative ways. As Rafael continues to develop this system (in close collaboration with a plant biologist, Dr. Leonie Moyle), it promises to be one where he will be able to produce new and exciting results on the evolution of sex chromosomes for years to come.

Rafael's new research has addressed multiple areas that benefit from his excellent quantitative skills, including the modeling and analysis of genetic interactions involved in species divergence. This has involved a number of different projects on this broad topic, but have all again demonstrated Rafael's ability to think clearly and creatively about problems in evolutionary genetics. So as not to belabor all of these projects (I'm sure his research statement describes them), I will just highlight two. One has involved a new way to understand the evolution of transcriptional regulation using nearly isogenic lines (NILs) and RNA-seq data in wild tomatoes. Rafael has shepherded two papers on this to completion: one in *Evolution* (Guerrero et al. 2016) and one in *BMC Plant Biology* (Broz et al. 2017; he is a co-first author). Rafael has done all of the computational and statistical work on these papers. In the second project (in sole collaboration with Dr. Leonie Moyle), Rafael developed a new mathematical model of genetic interactions among multiple loci causing "Dobzhansky-Muller interactions"; i.e. the loci causing reproductive incompatibilities between species. Dr. Moyle's lab had unprecedented data combining multiple NILs that individually cause incompatibilities, and Rafael has developed a framework for understanding what the results mean when multiple NILs are combined in a single genetic background. His work has led to a high-profile paper in *PLoS Genetics* (Guerrero et al. 2017). This work seems poised to put Rafael in a position to lead the way in developing the theory for understanding this type of data, more of which are sure to come. He is already working on this with a first-year student in my lab, who he is mentoring while I am on sabbatical.

In addition, Rafael has initiated a new project looking at maternal-fetal interactions in humans. I had been pulled into a large genome-wide association study (GWAS) on gestational diabetes by colleagues at our medical school, and was complaining about how boring GWAS was to Rafael. He immediately saw an opportunity to extend this work by genotyping the children of the women in the study, using the phenotypes available to understand the genetic basis for maternal-fetal interactions (and possibly conflict). We immediately took his idea to the consortium running this study, and Rafael's plan was approved! The genotyping work is ongoing, but Rafael's ability to: come up with an exciting research idea, put this idea into a written plan, and convince medical doctors that it would work, was truly impressive. It was very fun for me to just have been along to see these ideas develop.

On a personal level, Rafael is a friendly, outgoing scientist who clearly works well with collaborators and colleagues. I have had the opportunity to observe his exchanges with both students and faculty and have always been impressed by his ability to convey complex ideas with

clear, brief explanations. He has initiated collaborations with other faculty on his own (always mindful that I was okay with this), and I have encouraged him to do so. It is clear that they also view him as more of an equal colleague than as a junior, as do I. While I am on sabbatical he has become the temporary “head” of my lab, and I have the full confidence that he is capable of leading this group of postdocs, graduate students, and undergraduate students in my absence. He is clearly ready to run his own group.

Rafael has worked diligently to put himself in a position to succeed in a faculty job. I have no doubt that the multiple projects he is running will continue to bear fruit in the near future, and that this groundwork will ensure his continued success moving forward. In short, I believe he would make an excellent colleague and an exceptional addition to your faculty.

Sincerely,

A handwritten signature in black ink, appearing to read "Matt Hahn", with a stylized, cursive script.

Matthew Hahn