

New York University
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Department of Biology

1009 Main Building
100 Washington square East
New York NY 10003-6688

Claude Desplan

Tel: (212) 998 8218
Private Fax: (212) 995 4710
E-Mail: claudio.desplan@nyu.edu

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Faculty Search Committee
Prof. James Glazier
Dept. of Physics, Indiana University
Swain Hall West 117, Bloomington IN, 47405-7105

Re: Recommendation for Dmitri Papatsenko

Dear Committee Members:

This letter is a very strong recommendation for **Dmitri Papatsenko** who has applied to a position as an assistant professor in your department.

Dmitri has been a postdoctoral associate, and more recently an independent research fellow in my laboratory for the last five years. He came to my lab after completing his PhD at the Engelhardt Institute of Molecular Biology, one of the most prestigious institutions of Moscow. As soon as he joined us, I realized that he was a very strong scientist, having a combination of a very bright and independent mind and an ability to adjust to his environment. At the time, my lab was strongly directed toward developmental questions, although we had not started working on our current project: to understand how the *Drosophila* eye is patterned to achieve color vision. Our work now focuses on the two types of photoreceptors, R7 and R8, which express different opsins, the visual pigments that allow each class of photoreceptors in flies to compare their input for color discrimination. Dmitri was clearly more interested in the molecular and bioinformatics aspects of the work than in the developmental aspects, and his initial contribution was to characterize a new group of long-sought R8 opsins that detect blue or longer wavelengths. Although people had failed for over 10 years to find the R8 opsins, Dmitri rapidly characterized Rhodopsin 5. He discovered that this blue-type opsin was expressed in a stochastic array of R8 cells (about 70%). Interestingly however, was the fact that this opsin was always expressed in ommatidia (the unit eyes) that expressed a specific UV opsin, Rh3, in the overlying R7 cell. This was the first and critical step in a total change of research direction of my lab that is now over 80% dedicated to this topic.

Dmitri thus opened the field for us, and we owe him a great deal for this. It was clear, however, that he was more interested in the way these genes were regulated than by the physiology of the system. In fact, his interest was much broader than that, and his ambition was to understand how specific promoters are controlled to provide spatio-temporal expression. He realized that the genes that were studied in my lab and in that of Steve Small, out^r collaborator in the department, i.e. the *Drosophila* opsin and developmental genes, were the perfect tools to address these questions. For instance, the opsin genes are expressed with exquisite specificity, each in one subtype of photoreceptors with total exclusion of the others, and their expression reaches extremely high levels without ever spilling over; furthermore, these promoters are incredibly small and tight (~180bp) and we have sequences from 30 different opsin promoters from different species!

At this point, Dmitri undertook a significant change in focus, still keeping with the same biological system: Trying to understand the language of promoters. For this purpose, he started a collaboration with a very talented Russian colleague who provided the computing aspect of a new project and he took full advantage of his previous experience with transcription and with the opsin promoters. This, allied to the power of *Drosophila* genetics, allowed him to develop a system where *in silico* results could be tested *in vivo*.

Dmitri's basic idea was that it should be possible for any given gene from the many completed genome sequences, to rapidly identify its promoter and reach a good understanding of its regulation without going through the standard methods of extensive promoter bashing and sequence comparisons. The concept that he wanted to test is that functional regulatory binding sites in 'minimal promoters' have many 'shadow sites', *i.e.* statistically significant repeats with several mismatches in the neighboring area. These 'shadow sites' have been noticed by multiple investigators, but their significance has never been tested, nor have they been used for the identification of binding sites. Dmitri developed an algorithm to identify functional cis-acting sites using the very well known early developmental enhancers from *Drosophila* for which both binding sites and trans-acting factors are known. A paper describing the results obtained and demonstrating the feasibility of the approach, including a complete statistical analysis was recently published in 'Genome Research', the leading journal in the field of Genomics. He has since developed these ideas further with a study of clustering of binding sites and two other papers are submitted on this topic.

Dmitri developed this project totally independently from me, taking advantage of the lab environment and he is now the principal investigator, both intellectually and technically, for his sophisticated research program. This is such that he was appointed as an independent scientist in the department in a non-tenure track position, and he has submitted an RO1 application to NIH without my contribution. After this paper, I stopped putting my name on his papers as I am no longer part of his genomic investigations other than by providing financial support and a laboratory environment.

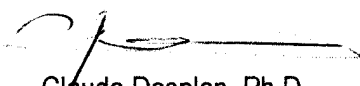
I hope that it is very clear from this description that I have the highest respect for Dmitri, and I give him full credit for the development of the genomics aspects of this project. When he leaves to take a faculty position, he will be able to take with him the entirety of the project and I am certain that he will succeed rapidly.

As a person, Dmitri is an extremely intelligent and dedicated scientist, who can develop tools from scratch, make the right contacts and establish collaborations in a very mature and passionate way. He has always been a major asset in the lab, providing critical understanding to everyone's project, with his view of biology that is significantly distinct from that of most other biologists. The conjunction of *in silico* approaches followed with tests *in vivo*, using the most sophisticated transgenic systems, is unique and an essential tool for his future success in Genomics.

I am therefore fully confident that Dmitri will become a very significant player in the field. He has already exhibited his skills as a group leader, with a full-time student working with him and several Master and undergraduate students who have performed very well under his supervision and can only speak highly of his directions. Dmitri is a well-rounded, well-liked and more importantly very intelligent and efficient scientist

Dmitri also conveys his enthusiasm in his seminars. While often handling complex material that is unfamiliar to the average biologist, he has now become able to convince them of the power of the approach; similarly, he can talk well to bioinformatics colleagues and he has become himself quite proficient with computer analyses. Dmitri is therefore a fully prepared independent investigator, who will very likely have soon secured his own funding and could rapidly start his lab using the small team that he has assembled at NYU. He has my highest support to obtain a position of Assistant Professor. His deep intelligence, energy and commitment will be great assets in the early stages of his lab.

Sincerely,



Claude Desplan, Ph.D.
Professor of Biology
Laboratory of Molecular Genetics