Washington University in St. Louis
SCHOOL OF MEDICINE

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Professor of Cell Biology and Physiology

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To members of committee for the starting faculty position in the National Centre for Biological Sciences (NCBS), a center of the Tata Institute for Fundamental Research (TIFR).

I am pleased to recommend Dr. Sumit Mukherjee for the faculty position in NCBS. My recommendation carries a high level of enthusiasm and support.

I met Sumit for the first time when he presented his doctoral studies during an postdoctoral interview for Dr. Dan Goldberg's lab at Washington University School of Medicine in St. Louis. He soon joined Microbiology Department as a postdoctoral fellow in the Goldberg Lab. Lab of Dan Goldberg lab and my lab have joined lab meetings and Sumit and members of my lab, including myself, interact on the weekly basis. During the joint lab meetings, we discuss projects, results, manuscripts in progress or presentations for the upcoming conferences, with an additional journal clubs covering novel published studies from other labs. I was involved in thesis committee of the graduate student that previously worked on the similar project in the Goldberg lab and I have good insight in both scientific and personal qualifications of Sumit as an independent scientist, member of Goldberg lab and WashU community.

Following Sumit's work over the last four years, I can conclude that Sumit is one of the rare scientist that has an interest in multiple disciplines. He is genuinely interested in bioinformatics, structural biology, biochemistry, biophysics and basic biology of parasites. In his doctoral and postdoctoral work, he combined and continues to use knowledge and methods from multiple fields in order to give a complete insight in the cellular process that he follows, regardless whether that is lipid metabolism in Leishmania or proteases in Plasmodium. He has chosen for his work in the Goldberg Lab to study proteases Plasmepsin X and Subtilisin like protease 1 (SUB1). In the first part of his postdoctoral work, first two years, he focused on the role of domains in the activity and function of Plasmepsin X protease. His studies resulted in two publications in Nature Communication and mBio journals, both with Sumit as leading author and leading researcher in the project. In the last two years of his postdoctoral work and with a funds of American Heart Association, Sumit focused on the study of the role of subtilisin like protease 1 (SUB1) in egress of Plasmodium from erythrocyte and connection of this protease with Plasmepsin X maturation. Some of these studies are still waiting for publication. While one can argue that he already has multiple publications that indicate his knowledge and experience, I would really like to point out that I have rarely seen that amount of maturity and thoughtfulness in the lab work and writing from any other postdoctoral fellow. He is already at the level of the independent investigator and probably a right person for the position that he applied at NCBS. If I would need to compare Sumit to other people that I knew I would rank him as high as Dr. Rachel Green's postdoctoral fellows Nicholas Guydosh or Kristin Koutmou, both successful investigators and tenured professors now at NIH and University of Michigan in Ann Arbor, respectively.

In the short description of Sumit's passion for the science and projects, I should point out that Sumit in the early days after joining Dan Goldberg's lab described function of Plasmepsin X in Plasmodium parasite. He showed that this aspartic protease, as a secreted protease, supports normal egress, invasion, and parasite growth. He was the first to describe that the intracellular pH is a critical regulator for Plasmepsin X activation. His findings unfolded the temporal, spatial and biochemical control of this unusual but important aspartic protease and he was chosen as a speaker with this research for Molecular Parasitology meeting at Woods Hole.

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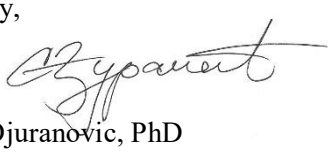
In parallel, while working on this manuscript Sumit started working on SUB1 and its role in egress of Plasmodium parasite from the infected host erythrocytes. SUB1 regulates the breakdown of both the parasitophorous vacuole membrane and the erythrocyte membrane but mechanism of its activation is unknown. Using bioinformatics analyses as well as a combination of biochemical and cell biological assays Sumit found that plasmepsin X can directly cleave pro-domain and additional form of SUB1 to make SUB1 fully active. By studying specific cleavage mutants in the parasites, he discovered a rather complex process of activation of SUB1 by plasmepsin X. These results were also a basis for the proposed research described in the Aims of his AHA project which was successfully funded. These aims were focused on defining the role and mechanism of SUB1 in the breakdown of the parasitophorous vacuole membrane during egress of Plasmodium falciparum. Describing the underlying mechanism of SUB1 will be the key to identifying new targets and developing novel drugs for treatment of malaria.

Besides working on plasmepsin X and SUB-1, Sumit has been active on side projects and he was and will be also a co-author on a publication from my group that will soon to be submitted in one of the highest ranked journals. One manuscript will define mechanism of novel peptide drug that targets late stages of Plasmodium life cycle in erythrocytes and potentially egress or re-infection. I think these points to his general interest in science and that he is a great lab and community citizen. He has developed great relationship with all people in the Goldberg and my lab. I find him to be highly intelligent, hardworking and motivated to succeed. He is enthusiastic and excited about his research. He clearly enjoyed short and long term challenges, issues and activities associated with laboratory research and his project in particular. During his work in the Goldberg Lab, Sumit was actively involved in mentoring both undergraduate and graduate students in the Goldberg Lab as well as in mine lab and he gathered lot of experience that will be useful for his role as an independent researcher and new assistant professor.

Overall, I recommend Sumit to you with great enthusiasm and no reservations. Thank you for your consideration of his application.

Sincerely,
Sergej



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