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Burroughs Wellcome Fund

Re: Reference for Jesse S. Wright for Career Award in Biomedical Sciences

Dear Members of the Review Committee:

It is with great pleasure that I provide my strongest support for the Dr. Jesse S. Wright for a Burroughs Wellcome Fund Career Award in Biomedical Sciences. I served as thesis advisor during his doctoral research at the University of Virginia. He demonstrated exceptional enthusiasm, imagination, dedication, and critical thought throughout his work here. His research dealt with the genetic and biochemical analysis of the regulation of the UhpB sensor kinase activity and regulation. Based on his performance here, I consider him a very promising young scientist who will make a strong impact in the area of bacterial signal transduction.

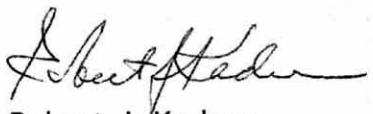
I was very impressed with his doctoral work in my lab, which was completely independent in design and implementation. He studied the transmembrane signaling process that controls expression of the UhpT sugar phosphate transporter in *E. coli.* UhpB is a transmembrane protein whose autokinase activity is regulated by the level of extracellular glucose-6-phosphate, sensed by the transmembrane regulatory protein UhpC. The crux of Jesse's work described the enzymatic properties of a soluble form of UhpB, lacking the transmembrane segments. The analysis of this unregulated but biochemically tractable form of the protein was needed as a preliminary to further studies of the coupled, membrane-localized process of transmembrane signaling. He used genetic and biochemical approaches to dissect the functional domains of the soluble C-terminal half of UhpB. The ATP-binding kinase domain near the C terminus can transfer phosphate from ATP to a crucial histidine residue located in a dimeric 4-helix bundle. He defined the conditions and role of specific residues in the bundle in phosphate transfer, dephosphorylation, and binding and transfer to the substrate protein, the transcription activator UhpA. He made important and novel findings regarding sequestration of UhpA by UhpB and of reverse phosphate transfer from UhpA to UhpB. This work led to a novel model for regulation of phosphate transfer through change in exposure of the histidine residue as a result of rotation of the helical bundles. Thus, he applied a wide range of genetic and biochemical approaches to this problem. This work has proven to be reliable and influential for our subsequent work on this system.

He chose to pursue postdoctoral training with Richard Novick at New York University. This choice provided him experience with a Gram-positive pathogen, and a different type of signaling process. It is clear from his productivity in this time that he continues his record of high innovation and achievement. His postdoctoral research remains in the area of bacterial signaling systems, but is quite distinct from his previous work and address an important topic of microbial pathogenesis. This work is quite interesting and novel and has provided him with a new set of experimental expertise. His accomplishments in fact sound quite exciting.

His work, like his personality, is marked with an exceptional degree of enthusiasm and energy. He was extremely well read in topics related to his research, and his experimental approaches were novel, independent, and convincing. He was a productive and independent investigator, who responded very well to advice and suggestions. He has a high degree of critical acumen in interpreting his results and designing further experiments. He is a bold and daring researcher with no reluctance to try new and risky experiments. In addition, he writes and communicates very well and present his results in a very clear and convincing manner, with wonderful graphics.

In summary, I offer my highest enthusiasm for his receipt of this award. I have no doubt that he will flourish and continue to develop as a leader in the area of microbial pathogenesis.

Sincerely,



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