



Timothy R. Hughes, Ph.D.

Professor, The Donnelly Centre for Cellular + Biomolecular Research

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August 1, 2017

Dr. Luis F. Larrondo
Departamento de Genética Molecular y Microbiología
Facultad de Ciencias Biológicas
Pontificia Universidad Católica de Chile
P.O. Box 114-D, Santiago, Chile

RE: Letter of Support for Grant Application by Dr. Luis F. Larrondo

Dear Dr. Larrondo, and to whom it may concern,

I am writing to express my support for the grant application, "**Millennium Institute for Integrative Systems and Synthetic Biology (MISSB)**" that you direct.

My group is interested in describing how genomes function on a global basis, by identifying, studying and mapping properties and relationships among individual functional units in the genome. For this, we employ diverse technologies, including, but not limited to, gene expression studies in several organisms, and importantly, global analysis of DNA and RNA binding activities. My group has considerable expertise in cutting-edge experimental approaches as well as on the computational data analysis required for the study of these complex biological processes.

As part of our global approach for characterizing the DNA binding preference of proteins across several taxa, an invaluable tool for the study of transcriptional regulation, we have been collaborating with Dr. Larrondo and his group to determine the sequence preference of all *Neurospora* DNA-binding proteins through a protein binding microarray approach – part of this work was featured in a collaborative publication in *Cell* in 2014.

I understand that you are now planning to design "orthogonal TFs" by transferring a given TF from one organism to another (that has no ortholog), and are also considering the possibility to change the binding specificity of existing TFs by altering the DNA binding domain, as well as designing synthetic promoters. These are exciting and challenging ideas, and I will be delighted to support these efforts as I can. Our ongoing offer to run Protein Binding Microarrays on constructs you generate still stands, and I will be happy to provide input on strategy for these new projects if you feel that would be useful.

Sincerely,

Timothy R. Hughes, Ph.D.
Professor