Here are a list of projects, at the interface of physics and biology, which should capture the interest of a young scientist who has the imagination and dedication to quantitatively explore and redefine new scientific frontiers.

Proposal: Genetic manipulation of a novel, early-branching organism to investigate animal origins

Supervisor: Dr. Steven S. Plotkin (Department of Physics and Astronomy, Genome Sciences and Technology Program, Bioinformatics Program, Institute of Applied Mathematics, UBC)
Co-supervision along with other faculty working in Molecular Genetics here at UBC is a possibility. This is the primary undergraduate project I will be focusing on this year.

Location: Chem/Phys Building, 6221 University Blvd, Point Grey Campus, UBC.

Description: In this experimental project, researchers will help establish and maintain multiple stable generations of ctenophores, a phylogenetically early-branching metazoan, in order to perform genetic manipulation on these organisms using CRISPR/Cas9 technology. Knock-outs and knock-downs of pluripotency factors and their inhibitors will first be implemented. Depending on our progress with this goal, we will then perform genetic knock-ins of fluorescent tags on histone proteins as proof-of-principle of transgenesis. Time permitting, we will then fluorescently tag stem cell pluripotency factors and their inhibitors, in order to monitor the spatio-temporal expression of stem cells markers during the development of this anciently-diverging animal.

For a student who likes working with computers, and enjoys writing pieces of code:

Proposal: Do proteins compensate energetically for the destabilizing effects of disordered segments?

Supervisor: Dr. Steven S. Plotkin (Department of Physics and Astronomy, Genome Sciences and Technology Program, Bioinformatics Program, Institute of Applied Mathematics, UBC)

Location: Hennings Laboratory, 6224 Agricultural Road, Point Grey Campus, UBC.

Description: Many proteins contain disordered loops in their native, biologically active structures. This project will employ computational modeling and molecular dynamics simulation to address a novel question in protein stability, namely how proteins might have evolved to account for the destabilizing effects of these disordered loops present in the native structural ensemble. Force is required to hold the ends of a polymer at a particular distance. We will investigate the hypothesis that proteins have stabilized the regions flanking disordered loops to account for this destabilizing effect. Preliminary results have shown that removing loop structures from a particular protein (superoxide dismutase 1) has lead to significant increases in the structural stability of the surrounding residues, but also an increased aggregation propensity for that protein. Here we will develop a protocol to automate the removal of loops from proteins, and measure the relative local stabilizing effects of interactions between amino acid pairs in both wild-type and loop truncated variants. We will employ both *in silico* force spectroscopy and statistical mechanics analysis to quantify these interactions. We will determine if loop stabilization is a universal feature across naturally-evolved protein structures, and why it might have occurred, as opposed to a mechanism that simply would have stabilized the loops themselves.