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THE UNIVERSITY OF BRITISH COLUMBIA

Department of Cellular and Physiological Sciences

Large-scale approaches to link genotype to phenotype

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Hosted by Dr. C. Loewen

12:30 pm,Thursday
October 20, 2016
LSC 3

Hundreds of thousands of genomes or exomes are sequenced each year. In order for them to be useful, we must understand the consequences of the variants we find, a step that remains a major challenge. Deep mutational scanning is a method that marries selection for protein function amongst a large library of protein variants with high-throughput DNA sequencing to measure the activity of hundreds of thousands of variants simultaneously. The result is a sequence-function map that describes the impact of all possible single and many double mutants on protein function. We have shown that sequence-function maps can guide the interpretation of coding variants in genomes and can be used to train computational predictors of variant effect. Sequence function maps can also teach us about protein properties like structure, aggregation, stability and enzyme mechanism and enable us to better understand protein evolution. Thus, they represent an important new tool for dealing with the deluge of variants we're identifying.