Genomes, Structural Biology and Drug Discovery: Exploring Chemical and Biological Space

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The knowledge that is now emerging from genomics of man and pathogens and from biochemical and structural biology programs has the potential to accelerate drug discovery.

Genome sequences, and most recently non-synonymous single nucleotide polymorphisms and somatic mutations, when taken together with structural and functional information on the gene products, can provide insights into the relationship of human genetic variation and disease. This is also helpful in identifying new targets for drug discovery; it is an exploration of biological space.

High-throughput biophysical and structural analyses can be used to investigate the chemical molecules that proteins might bind; this is an exploration of chemical space. I will argue that this is best achieved by structure-guided and fragment-screening techniques, which inform not only lead discovery but also optimization of candidate drug molecules.

My lecture will describe a multidisciplinary approach with physical, computational, chemical and biological techniques. I will describe recent developments both identifying targets and in making new medicines in academia through research programmes funded by the Gates Foundation, Wellcome Trust and EU and in a spin-out company (Astex Pharma). I will discuss applications in cancer and TB.