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Disease to therapeutics via 3D structures: stories from viral world

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Viruses are the smallest pathogens that pose serious health hazards to both, human and live-stock. There exists enormous diversity of viruses and viral epidemics cause huge disease burden. Vaccines have been developed to confer effective protection against several viruses. These vaccines were designed using conventional approaches wherein the whole pathogen (killed or attenuated) is used. Availability of three-dimensional (3D) structures of virus particles and viral proteins are proving to be a game changer for the development of new generation sub-unit vaccines. Similarly, 3D structures have also enabled development of anti-viral drugs to cure viral infections. However, there is an urgent need to broaden this scope to manage several emerging and re-emerging viral infections.

Designing the next generation drugs and vaccines against any virus necessitates detailed understanding of the structure of virion as well as the proteins it encodes. It is also essential to understand how viruses interact with their vectors and hosts during disease progression. Study of these interactions at the molecular level requires high resolution crystal structures (either in native or complexed forms) of viral antigens, the host receptors mediating viral entry and molecules of host immune system that confers protection against disease.

Three-dimensional structures serve as a starting point in various studies such as epitope mapping for vaccine design and pharmacophore mapping for drug design. The knowledge of 3D structures is also essential to study potential impact of mutations (variations) observed in the populations of viruses since they evolve at a very high rate. Such studies are required to prioritize targets for antiviral therapeutics and to design vaccines for the emerging seasonal infections. The structural data has also been instrumental to understand emergence of drug resistance as such strains have been attributed to lineage and population diversity.

Over the years, our group has explored both, sequential and structural space of viruses using the data generated through various omics technologies in general and structural genomics in particular. Various structural databases and tools that harness the power of 3D structures will be used to demonstrate how data in the public domain can be gainfully utilized for the development of anti-viral strategies.

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