Seminar Title: Discovering drugs, tools and interesting chemical properties
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Abstract: The discovery of small molecule drugs can be lots of fun. This seminar will show examples of scientific journeys taken from initial ideas to drugs in the clinic and to the market. A variety of examples will be shown on how initial leads were discovered then followed by structure- and dynamics-based design strategies to create potent inhibitors that target pathogens and cancer. An emphasis will be made on the exploitation of the bioactive ligand conformations using combinations of NMR, X-ray and computational tool methods. During these projects, we also noticed and exploited unexpected chemical properties. For example, unusual NMR spectra were observed for some compounds when dissolved in buffer, as a result of the formation of self-aggregates (nano-entities) of various sizes. These higher-order species were found to be implicated in side-effects such as immune responses, and can also serve as drug delivery systems. Other unusual NMR spectra were also noted for single molecules that were actually two or more as a result of chirality created due to slow or hindered axial bond rotations. The impact of these atropisomers on drug discovery were exploited as highly selective warheads and molecular switches. In summary, these and other observations demonstrate the importance of having fun and being creative at all levels of drug discovery and development.