Séminaire IBMM

Friday, September 12th 2014 – 10 to 11 am

Université Montpellier-1 **Faculté de Pharmacie** – Amphithéâtre **J**

Venoms to Drugs

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Many organisms including snakes, spiders, scorpions, cone snails, anemones and some mammalian species have evolved venom as either a defence mechanism or a weapon for prey capture. These venoms typically contain a complex cocktail of bioactive disulfide-bond rich small polypeptides which target a wide range of receptors including enzymes, ion channels, GPCRs and transporters. Of interest to drug designers is their high potency and selectivity combined with their resistance to many proteases.

These disulfide-bond rich toxins have small polypeptide chains typically between 10–80 amino acids that are highly constrained by two to five disulfide bridges and are structurally well-defined. Their high potency and *exquisite selectivity* has led to several drug candidates undergoing preclinical and clinical trials.

In this presentation I will describe the replacement of disulfide bonds by diselenide, thioether, triazole and selenoether bonds in highly bioactive toxins. This has led to mimetics that have similar or improved potency to the native molecule plus exceptional stability when exposed to reducing environments and in plasma. Together, these results underpin the development of more stable and potent peptide mimetics suitable for new drug therapies, and highlight the application of this technology more broadly to disulfide-bonded peptides and proteins.

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