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S E M I N A I R E

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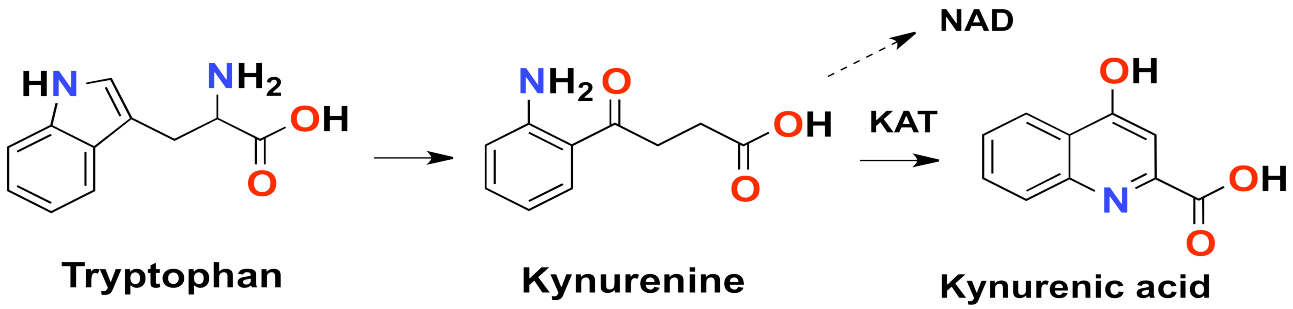
« STRUCTURE-BASED DESIGN OF KYNURENINE AMINOTRANSFERASE INHIBITORS: INFORMING AN UNDERSTANDING OF THE KYNURENINE PATHWAY »

The kynurenine pathway is a fundamental biochemical pathway, which begins with tryptophan and, in the brain, many of the ensuing metabolites are identified as either neuro-protective or neuro-active. We have been specifically interested in kynurenine aminotransferase (KAT) activity in this pathway, which converts kynurenine (KYN) to kynurenic acid (KYNA), and consider enzymes with this activity as potential drug targets to ameliorate neurogeneration and psychosis. We have now designed the most potent reversible inhibitors for both human KAT-1 and KAT-2, using structure-based methods, and our understanding of the inhibitory activity of the designed compounds specifically working on KAT-2. A fragment-library design approach has also been initiated which started with a diverse 1,000 compound set, which was screened using surface plasmon resonance, against immobilised KAT-2. We also report our specific results for the inhibitory activity of the estrogens with links to the observations of sexual dimorphism in schizophrenia. Our experiments continue to inform our design, with the potential for discovering further novel inhibitors.



Jeudi 10 octobre 2019
14h30
Salle de Conférences