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In This Issue

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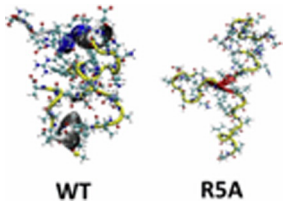
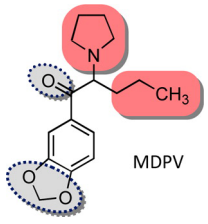
ROLE OF ARGININE IN AMYLOID-β STRUCTURE



Dynamic disordered protein amyloid-β (Aβ) is associated with Alzheimer's disease via aggregate formation. Previous studies suggest that arginine stimulates the Aβ assembly and show that an arginine (R) to alanine (A) mutation (R5A) decreases both aggregate formation tendency and toxicity. In the current issue, Coskuner and Wise-Scira (DOI: 10.1021/cn4001389) further investigate the roles of R and R5A mutation in the structures of Aβ42, the 42 amino acid residue alloform, which is reported to be the toxic protein.

The authors provide an atomistic level explanation for the reduced toxicity of the R5A mutant-type peptide in comparison to the wild-type Aβ42 peptide. The structural and thermodynamic properties of the wild-type Aβ42 peptide are greatly influenced by the R5A mutation. These results increase our fundamental understanding of the nature of the intrinsically disordered wild-type Aβ42 peptide associated with Alzheimer's disease, which could lead to the development of new drugs that target key residues promoting aggregation.

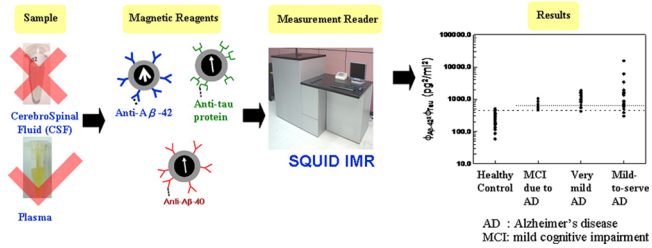
STRUCTURE–ACTIVITY RELATIONSHIP OF A COCAINE-LIKE DRUG



Methylenedioxypyrovalerone (MDPV) is a relatively new, yet widely abused, synthetic cathinone. Unlike other cathinone analogues that act as releasing agents at the dopamine transporter, MDPV is a dopamine reuptake blocker. In the current issue, Kolanos et al. (DOI: 10.1021/cn4001236) deconstruct the MDPV molecule to determine which structural features account for this blocking action.

The authors synthesized several MDPV analogues and compared them with MDPV in eliciting uptake inhibition of the dopamine transporter. All the analogues behaved as transport blockers. The presence of a tertiary amine or an extended side chain is sufficient to convert the cathinone analogues from dopamine releasing agents to dopamine blocking agents.

METHOD TO DIAGNOSE MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE USING PLASMA SAMPLES



In vitro diagnosis of Alzheimer's disease (AD) typically involves the detection of amyloids, tau protein, and their derivatives in the cerebrospinal fluid (CSF). Lumbar puncture is necessary for the collection of CSF samples, a relatively risky procedure. In the current issue, Chiu et al. (DOI: 10.1021/cn400129p) present a diagnostic method that requires plasma, a more reliable and convenient clinical sample.

The authors proposed a highly sensitive immunoassay to measure several biomarkers in plasma related to Alzheimer's disease. These biomarkers included Aβ40, Aβ42, and tau proteins. The samples used were from four groups: healthy controls, mild cognitive impairment (MCI), very mild dementia, and mild-to-severe dementia, all due to AD. The authors found that concentrations of both Aβ42 and tau protein for healthy controls were significantly lower than those of all the other groups. In addition, Aβ42 and tau protein concentrations in plasma were used to differentiate MCI from dementia both due to AD. Based on these findings, Aβ42 and tau protein concentrations could be exploited as plasma markers to differentiate healthy control patients and from patients with prodromal AD and AD-associated dementia.

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