Active compounds against Alzheimer's disease

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More than half of all cases of dementia in the elderly can be attributed to Alzheimer's disease. Despite vast research efforts, an effective therapy has not been developed, and treatment consists of dealing with the symptoms. Changes in brain tissues are a hallmark of Alzheimer's. In affected individuals, small protein fragments known as amyloid beta peptides accumulate and are deposited in the gray brain matter.

Researchers recently identified a series of synthetic compounds (inhibitors) that interfere with the self-assembly of the amyloid beta peptide in vitro; they influence both early stages and the transition to the characteristic amyloid fibrils. On a theoretical level, these compounds thus satisfy an initial condition for the development of an Alzheimer drug.

Peptide's disorder determines interaction

In order to understand the interactions between the amyloid beta peptide and active compounds at a structural level, Marino Convertino, Andreas Vitalis, and Amedeo Caflisch from the University of Zurich's Department of Biochemistry simulated these interactions on the computer. In doing so, they focused on a fragment of the peptide that is thought to control both interactions with inhibitors and progression of disease. Based on these simulations, the biochemists were able to identify a hierarchy of interaction patterns between the peptide and various active compounds. To their surprise, they discovered that the

disordered structure of the peptide controls the interactions.

"The peptide's disorder and flexibility enable it to adapt to many basic structural frameworks," explains Andreas Vitalis. Often it is only subparts of the molecules that mediate interactions on the compound side. However, even minimal changes to a compound may induce measurable changes to the peptide-compound interactions. "Design of active compounds that influence the amyloid beta peptide structurally in a specific manner will only be possible with the aid of high-resolution methods that are limited to one or a few molecules," concludes Vitalis. In the next step, the researchers from the University of Zurich want to identify new classes of active substances with controllable properties that interact with the amyloid beta peptide.

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