

Public Lecture by Dr. Edward Koo
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“Potential of Over-the-Counter Anti-inflammatory Drugs for Alzheimer’s Disease Treatment”
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Epidemiologic studies have shown that patients who are chronic users of nonsteroidal anti-inflammatory drugs (NSAIDs) have a reduced risk of developing Alzheimer's disease (AD). Many of the NSAIDs can now be obtained as over-the-counter medications. Whether this apparent risk reduction of AD is true has not been definitively established. Even if true, the mechanism by which NSAIDs protect against AD is unclear. For many years, many investigators assumed that this effect is due to an effect of these drugs on the chronic inflammatory responses that are always present in brains of AD individuals. Therefore, intake of NSAIDs would lower these brain responses and protect the individual from AD changes. While this may be true, studies carried out jointly at UCSD and with colleagues at Mayo Clinic, Jacksonville, showed that certain NSAIDs, including ibuprofen, sulindac, and indomethacin among others, preferentially lower the levels of one form of amyloid peptide in cultured cells and in brains of laboratory animals. The formation and deposition of amyloid in brain is believed by many investigators to represent an early and initiating event in AD. Therefore, we have proposed that this newly described activity of these drugs may be one explanation for the beneficial effects of NSAIDs against AD. Interestingly, this activity against amyloid is not present in all NSAIDs. Our results suggest that designing drugs or using currently available drugs that selectively target amyloid production may be one avenue to AD prevention or treatment.

In this talk, I will review the features of AD and discuss the amyloid theory of AD. This will be followed by reviewing the epidemiology results on NSAIDs and AD. I will then present the recent results of NSAIDs and amyloid reduction obtained in our laboratories. Finally, I will discuss completed and ongoing clinical trials of NSAIDs in AD, including a small Phase I trial with a novel NSAID analog currently ongoing at UCSD.