# 利用普利昂蛋白 E196 突變之聚集特性分析以進行黃酮類藥物篩選

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摘要:

普利昂疾病，又稱為傳染性海棉腦病（TSE），是一種致命的神經退化性疾病。人類的普利昂疾病有庫賈氏症 (CJD)、致命的家族性失眠症 (FFI)等，在動物方面有羊搔症、狂牛症。致病性的普利昂蛋白富有穩定的β折板結構，在腦部產生堆積後形成斑塊，導致神經細胞死亡。有研究顯示，普利昂蛋白 E196 的突變會產生結構的改變；相對於原生型態，E196K 的結構會較於鬆散，且在纖維核心的部分會由疏水腔變為親水腔。本研究團隊之前的研究結果顯示槲皮素與普利昂蛋白的 E196 緊密結合後可改變其纖維化的特性。原生型普利昂蛋白中，E196 帶負電荷，而 E196K 突變種帶正電荷，E196A 突變種為電中性。我們利用不同突變種探討電荷對結構及蛋白質特性的影響，進而檢視槲皮素與這三種電荷狀況之普利昂纖維的作用狀況。

黃酮類化合物是一類多酚類物質，廣泛分佈於植物中，具有很強的生物活性，包括抗氧化、抗癌、抗炎等作用，可預防神經退行性疾病。在普利昂蛋白聚集後加入盧丁、橙皮素、橙皮苷、槲皮素，再利用傳統蛋白質檢測法 ThT 螢光、內在色胺酸螢光、剛果紅染色、圓二色光譜儀、螢光顯微鏡及穿透式電子顯微鏡觀察蛋白聚集和藥物消除聚集的效果。更進一步，嘗試利用奈米銀之表面電漿共振性質經與蛋白質結合後所產生之不同頻率與不同波長訊號，作為一個奈米檢測平台，以達到快速篩選藥物的目的。

# Screening of Anti-Prion from Favonoids Based on Aggregation Properties of Prion E196 Mutants

Abstract:

Prion diseases, also called transmissible spongiform encephalopathy (TSE), are a group of fatal neurodegenerative diseases, including Creutzfeldt-Jakob disease (CJD), fatal familial insomnia (FFI) in human and Scrapie, bovine spongiform encephalopathy (BSE) in animals. Pathogenic prion proteins are rich of stable β-sheets. Their accumulation in the brain forms amyloid plaques leading to nerve cell death. Many researchers have found that the mutation of prion protein E196 changes the structure. Compared with the wild-type, the structure of E196K is looser, and the hydrophobic cavity of the fibril core turns hydrophilic. Our previous research showed that quercetin can change its fibrillization properties by tightly binding to E196 of prion protein. In the native prion protein, E196 is negatively charged, while E196K mutant is positively charged, and E196A mutant is electrically neutral. We use different mutants to investigate the effect of charge on structure and protein aggregation properties, and then examined the interaction of quercetin with prion fibrils in these three charged states.

Flavonoids are a class of polyphenols that are widely distributed in plants and have strong biological activities, including antioxidant, anti-cancer, anti-inflammatory effects, and can prevent neurodegenerative diseases. Rutin, hesperetin, hesperidin, and quercetin will be added after prion aggregation. Afterwards, traditional protein detection methods including ThT fluorescence, intrinsic tryptophan fluorescence, Congo red staining, circular dichroism spectroscopy, fluorescence microscopy and transmission electron microscope will be used to observe the effect of protein aggregation and disaggregation. Furthermore, the surface plasmon resonance properties of prion fibril bound nano silver will be measured for their sensitivity in signal frequency and wavelength. We expect to build a nano-detection platform for rapid drug screening.