Abstract of Lecture

Developing mRNA for Therapy

Messenger RNA was discovered in 1961 and it took 60 years until the first mRNA became FDA-approved product in the form of COVID-19 mRNA vaccine. During those years a lot of progress has been made by hundreds of scientists. First, isolated mRNAs were structurally and functionally characterized. In 1978 isolated mRNA delivered into mammalian cells were shown to produce the encoded protein. In vitro transcription - introduced in 1984 - made it possible to generate mRNA coding for any desired protein from the corresponding DNA by using phage RNA polymerases. In the early 90s in vitro-transcribed mRNA was mainly tested in animals as vaccine against infectious diseases and cancer. A great extent of progress toward a viable treatment was made during those years but the inflammatory nature of mRNA initially hampered its medical use. Together with my colleagues, we achieved a great milestone when we warded off the response by replacing uridine with pseudouridine in mRNA. We further demonstrated that modified mRNA formulated with lipid nanoparticles can be a potent vaccine. These discoveries eventually led to the development of the mRNA vaccine that has now helped to fight the global pandemic and opened the door for developing breakthrough therapeutics for incurable diseases and unmet medical needs.

講座摘要

研發信使核糖核酸作治療用途

儘管科學家在1961年已發現信使核糖核酸（mRNA）的存在，但要到60年後，美國食品藥物管理局才首次批准使用mRNA為疫苗，以應對2019冠狀病毒病。在這悠長的60年，數以百計的科學家在研發mRNA的過程中取得了不少成果。首先，科學家通過分離mRNA，成功描繪了它的結構和功能。1978年，他們將分離後的mRNA植入哺乳動物的細胞中，證實可以產生特定的蛋白質編碼。1984年，科學家引用離體轉錄的技術，成功利用噬菌體核糖核酸聚合酶，從相應的脫氧核糖核酸（DNA）中，製造所需蛋白質的mRNA編碼。90年代初期，科學家開始試驗以離體轉錄的mRNA置於動物體內作測試，為研發抵抗傳染病和癌症的疫苗鋪路。雖然爾後數年，這方面的測試取得了極大的進展，但mRNA對炎症反應的特性，仍窒礙了研究員嘗試將它轉化為醫學用的疫苗。其後在賓夕法尼亞大學研究團隊的協助下，我們通過將mRNA內的「尿苷」替換為「偽尿苷」，成功減退mRNA對炎症呈現反應的特性，結果令人振奮。經進一步的研發，我們證明利用脂質納米粒子配製的mRNA，經修葺後可成為一種非常有效的疫苗。這一連串的研發，最終導致成功開發應用於醫學上的mRNA疫苗，並適時用以協助抗擊肆虐全球的新冠病毒，同時亦為治療其他頑疾帶來新的希望，為開創嶄新的醫療用途打通開了突破口。