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Development of novel nanomedicines to inhibit pathological formation of amyloid plaques in Alzheimer's disease.

(supervisors Prof Tom Davis, Dr Aleks Kakinen, Dr Ibrahim Javed)

Alzheimer's disease (AD) is the most severe form of neurological disorder, characterized by the presence of extracellular amyloid-β (Aβ) plaques and intracellular tau tangles. Despite AD is becoming more prevalent as the population ages, yet the mechanisms that lead to synapse destabilization and neuron death remain elusive. Deposition of fibrillar plaques in the brain correlates with neurodegeneration and cognitive disfunctions in AD. The development of biocompatible nanomaterials has become a new frontier in the detection, treatment and prevention of human amyloid diseases. Researchers have investigated the interaction between Aβ and various classes of nanoparticles for controlling Aβ aggregation. This project aims to develop novel smart biocompatible nanomedicines to inhibit pathogenic amyloid plaque formation in AD using *in vitro* and *in vivo* disease models.

Understanding the effect of gut-bacterial amyloids on amyloid plaques formation in Alzheimer's disease.

(supervisors Prof Tom Davis, Dr Aleks Kakinen, Dr Ibrahim Javed)

Alzheimer's disease (AD) is one of the leading causes of dementia with tremendous socioeconomic impact. Despite AD is becoming more prevalent as the population ages, yet the mechanisms that lead to synapse destabilization and neuron death remain elusive. Deposition of fibrillar tangles and amyloid plaques in the brain derived from the aberrant aggregation of tau- and amyloid-β (Aβ) peptides correlates with neurodegeneration and cognitive disfunctions in AD. Notably, gut bacteria produce similar amyloid structures to support their biofilms. The interaction between bacterial amyloid fibril and Aβ has been hypothesized to accelerate AD symptoms. This project aims to study the interaction of bacterial amyloids with Aβ peptide. Potential strategies include investigation of cross-seeding, aggregation kinetics and fibril structural rearrangements of hetero-amyloid formations.

Translocation of bacterial amyloids from gut to the brain and its implications in Alzheimer's disease.

(supervisors Prof Tom Davis, Dr Aleks Kakinen, Dr Ibrahim Javed)

Deposition of fibrillar tangles and amyloid plaques in the brain derived from the aberrant aggregation of tau- and amyloid-β (Aβ) peptides correlates with neurodegeneration and cognitive disfunctions in Alzheimer's Disease (AD). Notably, gut bacteria produce similar amyloid structures to support their biofilms. The interaction between bacterial amyloid fibrils and Aβ has been hypothesized to accelerate AD symptoms. Certain bacterial proteins have potential to induce gaps in gastric epithelial cells. This can result in leak and transportation of gut-bacterial products into the blood or lymphoid tissues, and then to the brain. This project aims to study translocation of bacterial amyloids from gut to the brain using *in vitro* gastric epithelial cell model.

Development of novel nanomedicines against bacterial amyloids

(supervisors Prof Tom Davis, Dr Aleks Kakinen, Dr Ibrahim Javed)

Bacterial biofilms are formed by bacterial colonies to protect their integrity, quorum sensing, inter and intra colonial communication and to hinder the access of antibacterial drugs to the underlying bacterial cells. This further leads to the development of multidrug resistance, that is a global pandemic. The bacterial amyloids provide scaffolds for the deposition and strengthening of biofilms. Nanomedicine can provide opportunities to inhibit the bacterial amyloids and biofilms to enable the re-supply of antibacterial drugs to bacterial cells, addressing multidrug resistance and pathological implications of bacterial amyloids.

Development of superior sentinel lymph node mapping magnetic tracers for the clinical detection of lymph node metastasis

(supervisors Dr Ruirui Qiao, Prof Tom Davis)

Cancer metastasis occurs via migration of cancer cells through the lymphatic system. The possibility of early detection of lymph node metastasis shows a great potential for improving the quality of life for cancer patients and better prognosis. In order to improve the sensitivity of diagnosis, this project aims to develop biocompatible magnetometer probe that can specifically recognise the lymphatic metastasis, thereby providing an ultrasensitive technique for the transcutaneous detection of sentinel lymph node.

Engineered polymeric and inorganic nanoparticles and their interaction with vasculature in diseases

(supervisors Dr Ruirui Qiao, Prof Tom Davis)

Polymeric and inorganic nanoparticles-based drug delivery systems (DDS) have shown great promises in cancer therapy. However, the drug delivery efficacy largely relies on the effective extravasation of nanoparticles through the tumour microenvironment with abnormal vasculature. This project aims to develop surface engineering strategies for the preparation of polymeric and inorganic nanoparticles with optimised physiochemical properties for the increased drug delivery efficacy at the tumour site. The cellular interactions between the engineered nanoparticles and vasculature will be investigated for improving the extravasation efficacy in tumour models.