Lipofuscein as marker or player in accelerated cerebrovascular ageing in epilepsy?

Promotor: Prof. M. van Zandvoort, "Advanced Optical Microscopy", UM
Co-promotores: Dr. D. Kapsokalyvas, Department of Genetics and Cell Biology, UM; Dr. K. Rijkers, Department of Neurosurgery, MUMC;
Skill & materials: Two-photon laser scanning microscopy (TPLSM); Super-resolution microscopy (STED); Cell culture and differentiation; labeling; human epileptic brain tissue
Key words/sectors: 前沿技□ / Frontier Technologies; 生物技□ / Biotechnology; 基□ 研究 / Basic Research; 基础研究 / Basic Research; 人类健康与疾病的生物学基□ / Biological Foundations of Human Health and Diseases
Basic Hypothesis: Mitochondrial activity and LPF production in young epilepsy patients and healthy elderly are comparable.

Cells with mitochondrial dysfunction undergo increased oxidative stress, causing difficulties in degrading proteins and lipids, ultimately aggregating in autofluorescent lipofuscein (LPF) droplets. As mitochondrial functioning decreases during ageing, LPF is often seen as "ageing" product. In the last 5 years, 2 expertise groups, a clinical group on epilepsy surgery[1-4] and a research group on advanced optical microscopy[5-7], joined forces. Using microscopy and cutting-edge image analysis, we found LPF in pial arteries of young epilepsy (±20 years) patients, at levels that are normally seen in healthy elderly (>65 years)[8,9]. We are currently undertaking studies into the role of both microvascular changes[10,11] and mitochondrial mechanisms underlying increased LPF distribution in the development of epilepsy.

We are looking for a talented and dedicated PhD student to carry out, analyze, and interpret cell culture studies with cells from 1) healthy individuals, 2) patients suffering from non-treatable epilepsy, and 3) patients suffering from mitochondrial dysfunction syndromes (POLG1, ATP6, tRNA(Leu)). Fibroblasts, stem cells, smooth muscle cells, and pericytes will be analyzed before and after metabolic challenge (glucose/galactose replacement). Imaging of mitochondrial activity and network, sub-mitochondrial structure and DNA changes, and LPF production (autofluorescence) are essential. We will compare these aspects to their readouts in brain pial arteries and tissues from control and epileptic individuals. Tissues are obtained during the surgery these patients undergo to decrease symptoms.

The collaboration between University Hospital and Imaging laboratories offers unique possibilities for the candidate to work on the cutting edge of two disciplines, i.e., imaging and resective brain surgery.

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