Deciphering the role of the blood-brain barrier in uremic toxins-induced neuropathies

Objective

Chronic kidney disease (CKD) is estimated to affect more than 840 million people worldwide constituting a major global health crisis. Clinically, the number of CKD patients will continue to rise mostly because of the ageing population and the increased prevalence of comorbidities such as diabetes and hypertension. In Europe, around 100,000 million people are affected by it. According to the gloomy predictions, Europe is at risk of a dismal increase of CKD patients as well as costs to healthcare systems. Patients with advanced CKD display a loss of kidney function leading to a blood accumulation of, a.o. protein-bound uremic toxins (PBUTs) that are poorly eliminated by renal replacement therapies. This systemic retention known as the uremic syndrome affects other organs. Indeed, neurologic complications such as
blood-brain barrier (BBB) disruption have been reported in CKD patients. The BBB guarantees the exchange between the blood and the brain through a complex cellular organization and a diverse range of transport proteins mediates the movement of endo/exogenous compounds.

I hypothesize that impairment of kidney tubular functionality in CKD causes an alteration of BBB integrity and function. This results in an aberrant BBB pass-through of PBUTs as well as impacts BBB vectorial transport capabilities. This fellowship aims to develop an appropriate multi-organs-on-chip device to accurately describe (i) the impact of PBUTs on BBB integrity and functionality, and (ii) the involvement of kidney-brain axis dysfunction in PBUTs-driven BBB disruption. We will develop a bioprinting-based microfluidic BBB-on-chip to accurately study BBB permeability, architecture, and transport function. This device will be connected to our established proximal tubule-on-chip to form a robust (kidney-brain) multi-organs-on-chip system. This project will pave the way toward the establishment of new and effective CKD therapies, and an expert system for pharmacology studies in a near future.

**Fields of science**

natural sciences > biological sciences > biochemistry > biomolecules > proteins
medical and health sciences > clinical medicine > endocrinology > diabetes
natural sciences > computer and information sciences > artificial intelligence > expert systems
medical and health sciences > basic medicine > pharmacology and pharmacy
medical and health sciences > clinical medicine > nephrology > kidney diseases

**Keywords**

kidney-brain crosstalk, multi-organs-on-chip, biofabrication,
membrane transporters, uremic syndrome, blood-brain-barrier

**Programme(s)**

HORIZON.1.2 - Marie Skłodowska-Curie Actions (MSCA)  

**Topic(s)**

HORIZON-MSCA-2022-PF-01-01 - MSCA Postdoctoral Fellowships 2022
Call for proposal

HORIZON-MSCA-2022-PF-01

See other projects for this call

Funding Scheme

HORIZON-TMA-MSCA-PF-EF - HORIZON TMA MSCA Postdoctoral Fellowships - European Fellowships

Coordinator

UNIVERSITEIT UTRECHT

Net EU contribution
€ 187 624,32

Address
Heidelberglaan 8
3584 CS Utrecht
Netherlands

Region
West-Nederland > Utrecht > Utrecht

Links
Contact the organisation  Website  Participation in EU R&I programmes  HORIZON collaboration network

Other funding
€ 0,00

EC signature date 14 March 2023
Last update: 27 July 2023

Permalink: https://cordis.europa.eu/project/id/101107439

European Union, 2023