PROGETTI ERANET

TITOLO PROGETTO	CODICE PROGETTO	CALL SECTION	RESPONSABILE SCIENTIFICO	QUOTA IRCCS	DATA INIZIO	DATA FINE	ABSTRACT
Cerebrovascular-immune interfaces: searching for an immune signature coupling hypertension to cognitive dysfunction - ImmuneHyperCog	ERP-2020-24671161	ERA-CVD Joint Transnational Call 2020 "Prevention of Vascular Cognitive Impairment through Early Detection of Cardiovascular Diseases"	Giuseppe Lembo	250.000,00 €	01/05/2021	01/05/2025	Hypertension is widely recognized as one of the most impacting risk factors for cognitive impairment. While epidemiological associations strengthened this observation during years, mechanistic investigations that may unravel the pathophysiological basis of this detrimental relationship are just at dawn. In the last years, we became aware that immune system participates to onset of hypertension and related target organ damage. Several studies demonstrated that various players of innate and adaptive immunity shape the effect induced by hypertension in target organs. Despite protected by a unique vascular system, the brain is not an exception, suggesting that the crosstalk between peripheral and resident immune components may play a decisive role in the evolution of cognitive impairment in hypertension. The complexity of vascular and immune interactions in the brain are further enriched by cells lining the vasculature, like pericytes, and the neuronal network itself. Here we have combined the complementary expertise of our groups to investigate the cerebrovascular-immune interface in experimental hypertension, with unprecendented details. Transgenic animal models, advanced in vivo imaging, fate mapping studies and an innovative - experimental system to reproduce and study ex-vivo the interface established by immune and vascular cells in the cerebrovascular system will be merged in our ImmuneHyperCog strategy. In the end, we conceived a translational aim dedicated to investigating the correlation between the immune landscape and early markers of brain damage at MRI in patients.
Understanding the role of NeuroimmunoMetabolic axis in development of HFpEF – NeuroimmunoMetHF	ERP-2019-24486286	ERA-HEALTH Joint Transnational Call 2019 "Research targeting development of innovative therapeutic strategies for cardiovascular disease (CARDIOMOV)"	Daniela Carnevale	400.000,00 €	01/04/2024	31/03/2027	Hypertension is a leading cause of death and disability worldwide. The NeuroimmunoMetHF Consortium aims to provide a novel approach to prevent and treat Hypertensive Heart Disease(HHD) by considering the role of the neural and immune systems in shaping the cardiac metabolic environment. We propose to focus on three areas: identifying the peripheral neuroimmune circuits that contribute to HHD in pre-clinical murine models; examining the effects of lifestyle factors on the neural drive and immunometabolic pathways in HHD; providing proof-of-concept evidence of the effects of exercise training and bioelectronic interventions disrupting neuroimmune reflexes on HHD in mouse models. Lastly, we will investigate the relevance of our findings to human pathology. Specifically, WP1 will focus on identifying the neuroimmune circuits of the brain-spleen-heart axis that contribute to cardiac architectural modifications in pre-clinical murine models of HHD by reactivate/inhibit the brain-to-spleen connection. To investigate if cardiovascular challenges shape the peripheral neuronal response conveying on the celiac plexus, we will determine whether these neurons are functionally connected to cardiac ganglia. We will also investigate the immune cell populations and molecular mechanisms underlying the immune-mediated cardiac remodeling and the immunometabolic pathways involved in HHD. We will examine how disrupted circadian rhythms, metabolic stress, and obesity impact cardiac remodeling in HHD. Hypothesis: WP2 will focus on the effects of exercise training and bioelectronic medicine interfering with cardiac ganglion signaling in mouse model of HHD to prevent the development of cardiac inflammation and heart failure progression. Finally, WP4 will investigate the relevance to human pathology to provide a clinical translation of the findings provided by WP1-3. We will use epidemiological and genetic tools to study theimmunopathology of HF in the well-characterized cohorts of UK Biobank. We will investigate the immunometabolic context in human heart tissue from HF patients undergoing cardiactransplantation to validate the pathways identified in animal models.Our project will elucidate how the neuroimmune pathways might influence cardiac metabolic homeostasis to add important new mechanistic insights and implement innovative tools for tailored immunotherapies based on bioelectronic medicine

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