Identification of Molecular Factors Involved in Skin Vasculature Aging

INVENTION: Investigators in the Martin Hetzer laboratory at the Salk Institute have created in vitro 3D models of the human skin vasculature and developed a novel multi-analytical approach that allow the identification of changes in endothelial cell gene expression and barrier functionality. Moreover, their approach recapitulates key differences between the endothelium of young and old donors, hence representing a powerful tool to identify novel aging biomarkers for the skin.

Using such tools and approach, our Investigators have identified and validated new aging biomarkers of the aging human skin microvasculature. As a proof of concept, our investigators found that the external supply of one of the protein biomarkers can restore the functionality of old endothelial cells by strengthening inter-endothelial junctions. Additionally, such protein biomarkers can improve vascular permeability and counteract the decline in vascular function by reducing vessel permeability, which may lead to the development of therapies by replenishing the protein factors that are lost with aging vasculature.

APPLICATIONS:

- Tool to screen and identify novel biomarkers that can be exploited for the development of future therapeutics modulating the vascular function.
- Delivery of the combination of identified biomarkers/proteins (e.g., drug-release patches or topical cream) can potentially slow down the skin degeneration during aging and age-related skin disease.
- Development of diagnostics based on identified biomarkers for age-related skin conditions and diseases.

ADVANTAGES of 3D models:

- Allow functional and mechanistic studies of vascular endothelial cells (VECs) changes during physiological aging and pathological conditions affecting the vascular system.
- Reduce the number of animals and humans tested.
- Long-living models of the skin microvasculature.

BACKGROUND: The basic unit of the human skin microvasculature is composed of capillary vessels partially wrapped by supporting mural cells and surrounded by a network of collagen-secreting fibroblasts. Vascular aging correlates with the pathogenesis of a large spectrum of cardiovascular and non-cardiovascular diseases. However, factors that drive the age-dependent decline of vascular structure and function remain largely unknown, mainly due to the absence of effective strategies to characterize and modulate features of the human vasculature.

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