



**Research Assistant:**

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**Research topic:**

Targeting skin metabolic activity to correct depigmentation in vitiligo: focus on IGF/Insulin signaling and glucose metabolism to prevent inflammation and immune system activation (PNRR-MCNT2-2023-12377707)

**Abstract:**

Vitiligo (VTG) is a skin condition characterized by lesions induced by autoreactive CD8+ T cells, which destroy melanocytes, leading to a loss of pigmentation and consequently the formation of white patches on the skin. VTG impacts the quality of life of affected individuals and sometimes results in the development of depression due to social stigmatization. To date, the pathogenesis of VTG has not been completely clarified, but several factors are considered responsible for its onset, including genetic predisposition, oxidative stress, triggering events such as stress, skin trauma, exposure to chemical agents, and certain medications. Furthermore, although various therapeutic protocols have been proposed to arrest the depigmentation process and stabilize the disease, a treatment that allows for long-lasting clinical results is not currently available.

Recent studies have shown that VTG is not just a skin disease, but rather a systemic condition that phenotypically manifests as pigmentation loss. Patients affected by this disease show metabolic alterations, albeit to a modest extent, especially in terms of lipid profile and insulin resistance in dermal and epidermal cells.

The project, proposed and funded by the Ministry of Health, aims to clarify the pathogenetic mechanisms of the disease and provide robust evidence supporting the treatment of VTG as a metabolic disease. The aim is to identify the metabolic modifications that trigger the inflammatory/immune process underlying VTG.

To do this, the plasma metabolic profile of patients with VTG will be evaluated, with a particular focus on the metabolism of sugars, fatty acids, and amino acids, and compared with the profile of a control cohort. This analysis, in addition to defining etiopathological mechanisms and identifying therapeutic strategies, will be potentially useful for identifying serum biomarkers of disease activity.

Furthermore, interleukins and cytokines involved in the inflammatory process will be quantitatively analyzed using immunoenzymatic methods. Circulating mitochondrial DNA, which results altered in VTG, will be quantitatively assessed using real-time PCR, along with its ability to regulate the phenotypic maturation of dendritic cells, through the phenotypic characterization of the dendritic cells themselves.

This independent, multicentric study, with a duration of 24 months, includes two cohorts: 239 patients and 239 controls, matched to the patients for sex and age. It involves prospective enrollment and the collection of biological material (peripheral blood) by combining a multicenter case series obtained from four Italian dermatology institutes: Istituto San Gallicano, IRCCS; Istituto Dermatologico dell'Immacolata, IRCCS; the Dermatology Clinic of the University of Cagliari; and the V. Fazzi Dermatology Department in Lecce.

The Cagliari unit, whose Principal Investigator is Professor Laura Atzori, will serve as a recruiting center and will be responsible for the metabolomic analysis of the collected plasma samples.



**Bibliography:**

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