

## **Maintaining Immune and Mitochondrial functions in Old adults with SAfe nutrition: the MIMOSA study**

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**Background:** The reduction of appetite and food intake is frequent in old adults and has been defined as “anorexia of aging”. It has multiple causes and finally results in malnutrition. Aging is associated with an imbalance in protein metabolism with increased catabolism, decreased anabolism and reduced splanchnic extraction of amino acids. Thus, both intrinsic and extrinsic factors contribute to malnutrition in old adults, which alters muscle mass and immune system health, and finally cause physical frailty. The Immune system changes with aging, with the development of an increased inflammation named “inflammageing” and an altered immune response. When inflammation and oxidative stress exceed a certain threshold, aging turns into senescence and “healthy” aging turns into “unhealthy” aging, with healthy muscles turning into sarcopenic muscles. Aging is associated with a decreased mitochondrial bioenergetics ability and with a consequent increase in oxidative stress. Mitochondrial dysfunction may explain the complex relationship between malnutrition, sarcopenia, immune dysfunction, and aging. Nutritional modulation of oxidative stress and of the mitochondrial function is possible: the administration of branched chain amino acids (BCAA) has already been shown to improve muscle health, mitochondrial function, and oxidative state in elderly malnourished patients. In addition to the above, deficiencies of several micronutrients are frequent in old adults, and particularly affect vitamins A, D, E, C, B-12, and zinc, but also omega-3 fatty acids, the latter being required for immunomodulation.

**Aim:** The present study will test the hypothesis that in malnourished patients hospitalized in a geriatric rehabilitation unit, a nutritional intervention combining BCAA and selected micronutrients, delivered orally for 6 weeks (but at least 21 days) may improve the nutritional status and its clinical consequences, namely sarcopenia and impaired immune function through modulation of the mitochondrial bioenergetics, oxidative state, inflammageing and innate immune defence.

**Study design:** prospective parallel, randomized, controlled, double blind trial

Randomisation into 3 groups: 1) control: protein oral nutrition supplements (ONS), 2) BCAA + protein ONS, 3) Micronutrients + protein ONS

Patients: malnourished patients aged  $\geq 75$  years, with an MNA-SF  $< 17$  hospitalised in a geriatric rehabilitation unit after discharge from an acute unit. N= 240

Primary endpoints: mitochondrial bioenergetics and redox state

Secondary endpoints: muscle mass, strength and function, phase angle, inflammation and immune response, patients' global health

Methods: Nutritional status by MNA-SF, Muscle mass assessed by Bioimpedance with phase angle, Nutritional requirements by Indirect calorimetry, Muscle strength by handgrip strength and muscle performance by the Short Performance Physical Battery (SPPB).

Timing of study visits: admission, at the end of stay (3 weeks), then at one and two months.

Laboratory investigations will address mitochondrial bioenergetics, biogenesis and fusion, Redox state by the thiometabolome, the immune system by lymphocyte answer to immune stimulation and immune cells metabolism, inflammation markers (hsCRP, IL-6), and micronutrients status by the respective blood levels.

Duration of the study: enrolment 2 years (+1 year for data handling)

