The European Challenge for Healthy Ageing (ECHA): Children and nephews of long living

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Healthy ageing is a major socio-economic challenge for the European Union. In fact, after the increase of life expectancy achieved in the last decades, the next goal in Europe should be to increase the **active life expectancy** (healthy ageing). Recently, geriatric and gerontological research have focused on critical factors leading to the loss of autonomy in late life. This holistic approach tries to evaluate the old person as a whole, and is not focused on single diseases. Even more important, the major message of gerontology and geriatrics is that the assessment of older persons cannot be limited to the medical aspects but should also involve functional assessment either of the motor ability or the cognitive ability, as well as of the social network of support and psychological component that may influence the quality of life in old age. From this perspective the fundamental concept of ***frailty*** **is emerging as a major characteristic of elderly people**, profoundly correlated with the ageing process. Despite the well recognised methodological difficulty related to an unequivocal definition of the term, recent literature has identified possible standardised functional criteria, as well as haematological and biochemical parameters, that at present can be taken as reliable markers of frailty. **Thus, a major target of the research on the determinants of the quality of life of old people should be to improve the criteria to define frailty, and to identify the major components of this syndrome**.

Schematically the major components that can be envisaged to play a role in frailty are environment and genetics. The data on this critical point are lacking and at present it is not possible **to quantify the contribution of genetics to frailty**. In this proposal we would like to address just this question, taking advantage of the results emerged from studies on human longevity. It is known that age of death of the parents of centenarians in good shape is significantly higher than that of people belonging to the same cohort, suggesting that a genetic component is associated with successful ageing. Thus, the prediction is that the children of centenarians will be more robust and less frail, according to functional assessment and a variety of haematological and biochemical parameters. Therefore, using an *ad hoc* design for the recruitment of the centenarians' children and their controls, **we will try to correlate the possible different frailty to genetic markers of candidate genes**, which the literature suggests to be associated with longevity. **The genes will be considered are those which play a major role in the capability of individuals to cope with stress.** This approach is in line with a major outcome of gerontological research which suggests that longevity, from model systems (yeast, nematodes and mice) to humans, appears to coincide with the genetic capability to neutralise damaging agents and to cope with stressors. Eventually, we should be able to identify a major component of frailty in humans, and to relate this phenotype with genetic markers. In this way **it should be possible to outline appropriate risk profiles for single individuals from a certain age onward**.

As the genetic and environmental components of frailty can vary substantially among European countries, three different populations of elderly people from **Italy**, **France** and **Denmark** will be enrolled and compared. This approach should allow us to answer another **fundamental question** related to the quality of life of the EU citizens, i.e. **are the frailty components similar in different countries?**

The advantage of such an approach is that the problem of frailty in the elderly is directly investigated in humans. More importantly, possible strategies for the utilisation of these scientific results by policy makers are envisaged.