MAPPING OF THE HUMAN PROMOTER OF GNB2L1 GENE ENCODING THE RACK1 PROTEIN AND ITS REGULATORY ROLE IN THE IMMUNOSENESCENCE

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The immunosenescence is a natural aging process of the immune system. The most relevant anatomical changes are the involution of the thymus and the lowered output of T lymphocytes. By a molecular point of view very little is known about the bases of the immune aging. Recently TLRs (Toll Like Receptors) have been described to be the major molecular actors of the innate immune response (1) and their altered expression has been correlated with senescence (2). Active PKCs take part into the TLRs signalling pathway (3) that is reported to trigger the activation of NF-kB and its translocation to the nucleus, where is able to activate different immuno-responsive genes. RACKs are Receptors for Activated C Kinases belonging to a little family of intracellular WD40 scaffold proteins and are able to actively participate in this process of signalling by modulation of active/inactive state of different PKCs (4). In particular TLR-4 is responsive to LPS (lipopolysaccharide; Gram-negative bacteria) and is able to produce macrophage activation (5). During last years our group gathered different results confirming a decrease of RACK1 protein during the aging with an altered interleukins secretion in rat alveolar macrophages (6), in the blood of AD (7) and aged healthy patients (8) and this well correlates with physiological decrease of DHEA (dehydroepiandrosteron). GNB2L1 gene encoding human RACK1 was recently cloned (9) and here we report the first mapping of its promoter region. We used different deletion mutants cloned in a new luciferase reporter Gateway® vector developed by us to accelerate promoter studies. With this new technique we'll be able to fast test different new constructs in order to capture DHEA responsive *cis*-acting elements. These sequences could open a novel farmacogenomic scenario for the treatment of elderly subjects that are less immunoreactive probably because of their low levels DHEA.

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