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*Approaching the new era of molecular medicine:
from target based agents to nucleic acids
in the treatment of tumours and neurodegenerative diseases*



ABSTRACT FORM

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Abstracts submitted for 28th Annual Conference of Italian Association of Cell Cultures (ONLUS-AICC) must be written in English.

RELATIONSHIP BETWEEN POLYMORPHISMS OF TAS2R38 BITTER TASTE RECEPTOR AND CHRONIC UPPER AIRWAY INFECTIONS

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The presence of taste receptors in extra-oral tissues may suggest additional roles apart from taste perception. Recently, an increasing number of reports demonstrated that the bitter taste G-protein coupled receptors family T2R, expressed in ciliated epithelial cells of the respiratory tract, are able to detect bacterial products and to stimulate innate immune defense against pathogens. Most microbial agents, secrete chemical signals known as quorum-sensing molecules that regulate the expression of genes involved in biofilm formation, virulence and other vital processes for microorganisms. Among the quorum-sensing molecules, the AHLs produced by *P. aeruginosa*, activate the receptor for bitter TAS2R38 expressed in ciliated epithelial cells of the respiratory tract, whereas mutants of *P. aeruginosa* lacking the AHL are not able to activate it. The activation of the receptor results in an increase of the Ca²⁺ flow and the ciliary beat frequency, as well as stimulating the production of NO which acts as a bactericide against the pathogen. The Caucasian population express three common polymorphisms (Pro49Ala, Ala262Val, Val296Ile) for TAS2R38 that lead to two major haplotypes PAV and AVI. The expression of either haplotype gives respectively 2 forms of receptors— functional or non-functional— i.e. unable to respond to specific agonists such phenylthiocarbamide and propylthiouracil (PROP). The two haplotypes PAV and AVI segregate into two major phenotypic classes: the "functional", sensitive to bitter, are homo- or heterozygous for the allele PAV, the "non-functional", are homozygous for the allele AVI. The genetic variations of the receptor TAS2R38 that affect sensitivity to bitter taste can help determine individual differences in susceptibility to bacterial infections of the respiratory tract allowing to plan a "target therapy". Cellular cultures from homozygous PAV/PAV individuals showed a more effective NO production, mucociliary clearance and bactericide effect than cultures from AVI/PAV or AVI/AVI individuals. As a consequence it is reasonable to assume that patients with genotype AVI/PAV or AVI/AVI are at greater risk of contracting infections from gram-negative, compared with homozygous PAV. Some authors have studied the correlation between genotype and microbiological results TAS2R38 tissue of respiratory mucosa. The result of this analysis proved to be very interesting, because it showed a

significant difference in the frequency of non-functional (AVI) than functional (PAV) among patients whose cultures were positive for Gram-negative bacteria, including *P. aeruginosa*.

The aim of the study was to characterize phenotypically the sensitivity to PROP and the receptor polymorphisms of TAS2R38, in patients with chronic or recurrent infections of the upper respiratory tract to identify high risk patients. The identification of high-risk individuals would allow to draw up protocols for specific follow-up and appropriate "target therapy".