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(71) Applicant *(for all designated States except US)*: **AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH** [SG/SG]; 1 Fusionopolis Way, #20-10 Connexis, Singapore 138632 (SG).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **REVERSADE, Bruno** [FR/SG]; c/o Institute of Medical Biology, 8A Biomedical Grove, 05-39 Immunos, Singapore 138648 (SG). **MUNDLOS, Stefan** [DE/DE]; c/o Institut für Medizinische Genetik, Charite Universitätsmedizin Berlin, Campus Virchow, Augustenburger Platz 1, 13353 Berlin (DE).

(74) Agent: **SCHIWECK, Wolfram**; Viering, Jentschura & Partner LLP, Rochor Post Office, P.O. Box 1088 Rochor Road, Singapore 911833 (SG).

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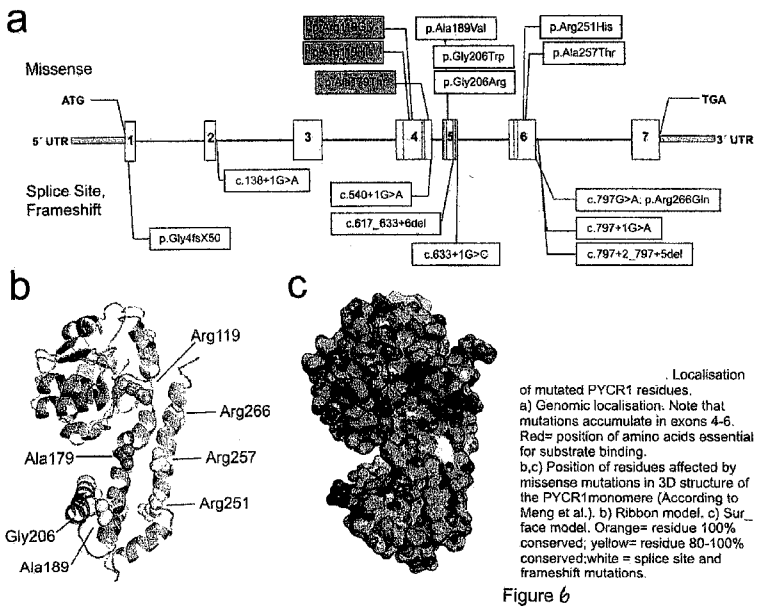
(54) Title: MUTEINS OF THE PYRROLINE-5-CARBOXYLATE REDUCTASE 1



. Localisation of mutated PYCR1 residues.
a) Genomic localisation. Note that mutations accumulate in exons 4-6. Red= position of amino acids essential for substrate binding.
b,c) Position of residues affected by missense mutations in 3D structure of the PYCR1monomere (According to Meng et al.). b) Ribbon model. c) Surface model. Orange= residue 100% conserved; yellow= residue 80-100% conserved;white = splice site and frameshift mutations.

Figure 6

(57) Abstract: The invention relates to muteins of the pyrroline-5-carboxylate reductase 1 (PYCR1), to nucleic acid molecules comprising a nucleotide sequence encoding such muteins, to methods of determining in a subject a predisposition of having an age related disorder associated with PYCR1, to methods of identifying a compound capable of modifying the expression of PYCR1 and methods of treating a subject having an age-related disorder associated with PYCR1. The invention further relates to a genetically modified animal and a method of modifying the expression of the PYCR1 gene in an animal.

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