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Genetic manipulation-free generation of human induced pluripotent stem cells capable of differentiation *in vitro* and *in vivo* into cell type of all three germ layers

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The reprogramming of human somatic cells holds great promise for treatment of human diseases, as well as attending immunological problems related to use of human embryo for the derivation of human pluripotent stem cells. However, low efficiencies of current reprogramming methods, immunogenicity and lack of understanding of molecular events, underlying the reprogramming mechanism which occur via many pathways that do not always lead to pluripotency, limits their utilization and raises questions regarding safety for therapeutic application. We report here about recently described human GPI-linked glycoprotein ACA involved in developmentally conserved signalling pathway(s) known to shape the structure of embryo, but influencing somatic stem cells compartments as well. ACA signalling induces via IP3K/Akt/mTOR sustained de-differentiation of blood progenitor cells leading to generation of ACA pluripotent stem cells. These cells do not form premature tumors (teratoma), a characteristic of embryonic (ES) or induced pluripotent stem cells (iPSC), but differentiate *in vitro* and *in vivo* into cell types of all three germ layers. Our results revealed insight into the molecular events that regulate cellular reprogramming suggesting that pluripotency might be controlled *in vivo* through binding of a natural ligand(s) to ACA receptor determining the level of de-differentiation and consequently the fate of stem cells, thus controlling the balance between renewal and differentiation, a process that might be responsible for replenishment of stem cell pool in the human body. Use of ACA pluripotent stem cells could help omitting cytotoxic preparative regimens explored usually for *in vitro* transfection conditions used thus far for generation of iPSC, and may enhance tissue regeneration via ACA's mechanism, to clinically useful level.

Biography

Zorica Becker-Kojić has Bachelor in Chemistry at University of Belgrade, earned PhD at University of Heidelberg, Germany. During her career she had held a senior research positions at the University of Heidelberg, Germany, University of New York, USA, Centro de Investigacion Principe Felipe, Valencia Spain, as well as teaching position at Mannheim University of Applied Science, Germany. She holds two international Patents related to Novel Human GPI-linked Protein ACA and its role in the regulation of self-renewal from adult to embryonic human stem cells. Currently, she is Co-founder and the leading scientists at R&D Centre for Autologous Adult Stem Cell Therapies, Heidelberg, Germany.

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