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Human Cardiopoietic Amniotic Fluid cell population: characterization and terminal differentiation

Barbara Ghinassi[1], Maria Angela D'Amico[1], Pascal Izzicupo[1], Simone Guarnieri[2], Maria Addolorata Mariggiò[2], Ivana Antonucci[3], Liborio Suppia[3] and Angela Di Baldassarre[1]

[1] Dipartimento di Medicina e Scienze dell'Invecchiamento, Università "G.d'Annunzio" di Chieti-Pescara, Italia
[2] Dipartimento di Neuroscienze, Imaging e Scienze Cliniche, Università "G.d'Annunzio" di Chieti-Pescara, Italia
[3] Dipartimento di Scienze Psicologiche, della Salute e del Territorio, Università "G.d'Annunzio" di Chieti-Pescara, Italia

Rationale. Human amniotic fluid-derived (hAF) stem cells are considered a novel class of multipotent stem cells, sharing characteristics of both embryonic and adult stem cells. In fact, they proliferate rapidly, are able to differentiate into cells of all the embryonic germ layers, but do not form teratoma. It has been already reported that the embryoid bodies (EBs) obtained from hAFs have a cardiac potential, but it has not been described a functional terminal differentiation in cardiomyocytes (CMs) yet.

Objective. Aim of this study was to foster the cardiomyogenic potential of hAFs in order to obtain a cellular population with morphological and functional features of CMs.

Methods and Results. AFCs were exposed sequentially to inducing factors (Ascorbic Acid, 5-Azacytidine, BMP4, ActivinA, VEGF) up to 15 days and differentiation was monitored. Only the hAF samples expressing the multipotency markers SSEA4, OCT4 and CD90 (CardiopoieticAF) responded to the differentiation process loosing their stemness and increasing the cardiac nuclear factors NKX2.5 and GATA4. After the differentiation cells expressed high levels of the sarcomeric proteins (cTnT, αMHC and αSA), the gap junction marker Connexin43 and both atrial and ventricular markers; moreover, up to 90% of the cells was positive for CACNA1C and SERCA2a, cardiac calcium pumps involved in the excitation/contraction coupling, and about 30% of the CardiopoieticAF-derived cells presented spontaneous intracellular Ca2+ waves and Ca2+ fluctuation in response to caffeine or adrenergic stimulation. Some spontaneous beating foci were also observed.

Conclusion. Our results demonstrate that CardiopoietichAFs can fully differentiate into a homogenous population of CM-like cells, characterized by cardiac-specific molecular, structural, and functional properties. Thus, CardiopoietichAFs can hold great promise for the development of in vitro models of cardiac genetic disorders, for drug discovery and testing, and for the emerging field of cardiovascular regenerative medicine.