Vascular cells derived from Hutchinson-Gilford progeria syndrome (HGPS) inducible pluripotent stem cells

Patricia R. Pitrez

MIT Portugal Bioengineering Systems, Biological Engineering, IBB Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, University of Minho, Portugal
pitrezpatricia@gmail.com

Background: MSc. in Biological Engineering, University of Minho, Portugal
Starting year: 2010
Research team: Helena Vazão[1] , Xavier Nissan[2]
Supervisors: Lino Ferreira[1], Isabel Rocha[3]
[1]CNC - Center of Neurosciences and Cell Biology, University of Coimbra, Coimbra, Portugal
[2]CECS, I-STEM, AFM, Institute for Stem cell Therapy and Exploration of Monogenic diseases, Evry cedex, France
[3]IBB – Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, University of Minho, Braga, Portugal

OBJECTIVES

To study the vulnerability of smooth muscle cells (SMCs) in Hutchinson-Gilford Progeria Syndrome (HGPS).

WORK PLAN

Hutchinson-Gilford Progeria Syndrome is a rare, progressive premature aging disease in children that leads to vascular SMCs degeneration and premature atherosclerosis.

Death occurs at a mean age of 13 years, usually from heart attack or stroke. One of the hallmarks of the disease is the dramatic loss of vascular SMCs in large arteries. In consequence, the arteries undergo vascular remodeling and calcification. So far, it is unclear the reason underlining the sensitivity of SMCs in the context of the disease.

To clarify the mechanisms behind SMCs loss, it's important to have human HGPSSMC; however, these cells are difficult to obtain from Progeria patients. Therefore, we derived HGPS induced pluripotent stem cells (iPSCs) from skin fibroblasts and then differentiate them into SMCs.

RESULTS

In this work, iPSCs obtained from HGPS fibroblast patients were successfully differentiated into HGPS-SMCs. These HGPS-SMCs showed impaired maturation and an upregulation of progeria markers when comparing with SMCs differentiated from healthy iPSCs. HGPS-SMCs shared similar features observed on progerin-expressing cells such as activation of several effectors of NOTCH signaling pathway and response to farnesyltransferase inhibitors. Therefore we have developed a cell model that is suitable for drug screening and to study the mechanism of SMC loss. This finding opens new opportunities for the treatment of HGPS disease and diseases related to vascular ageing.