Potential of Induced Pluripotent Stem Cells (iPSCs) for modeling and treating age-related human diseases

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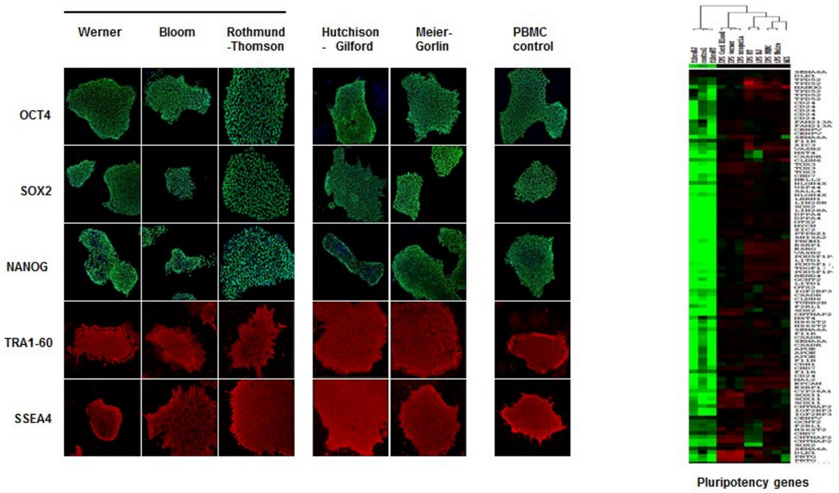
SUMMARY :

Helicases are enzymes involved in the replication, transcription and repair of DNA. Their deficiency is responsible for clinically identified syndromes: Bloom syndromes, Werner and Rothmund-Thompson syndrome. All are characterized by a strong predisposition to cancer and by a phenotype of premature aging of the affected persons. If the genes involved in these pathologies are identified, little is known about the mechanisms responsible for cellular senescence and genome instability. For these 3 pathologies, no therapeutic, preventive or curative solution has been proposed. Because animal models and differentiated cell studies are incomplete, the study of stem cells in these patients is essential. Recent technological innovations make it possible to reprogram somatic cells into induced pluripotent cells (iPS): this is an approach of choice to study the pathophysiology of a syndrome, to obtain differentiated cells of for disease recapitulation and to carry out the screening of Pharmacological active ingredients.

Our project is to generate iPS lines of 3 helicase-linked early aging syndromes from PBMC. We will study recapitulation of cellular related physiology and cellular senescence after their differentiation into Mesenchymal stem cells and their potential derivatives.

This project will enable us to create for the first time iPS cell lines for the pathologies of premature aging linked to helicases. Through these, it will be possible to study directly the cellular and molecular mechanisms, in particular the senescence and the genomic instability. The availability of these lines makes it possible to envisage the screening of therapeutic compounds which can correct the dysfunction of the cells.

ILLUSTRATION :



Desprat et al. unpublished results

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