PhD Open Days

Deciphering the cellular crosstalk in the bone marrow microenvironment of acquired aplastic anemia towards the expansion of transplantable hematopoietic stem/progenitor cells.

BIOTECnico – Biotechnology and Biosciences

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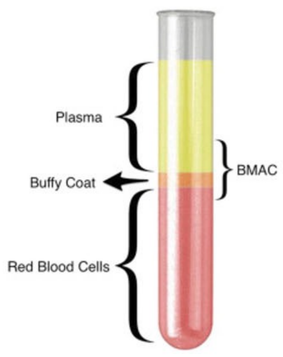
MOTIVATION

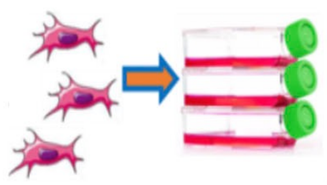
Acquired aplastic anemia (AA) is a rare disease characterized by a bone marrow hypocellularity, in which hematopoietic cells are replaced by fat cells, resulting in severe reductions in the numbers of hematopoietic stem/progenitor cells (HSPC). The incomplete understanding of AA pathogenesis, namely concerning the role of the BM microenvironment, which comprises mesenchymal stromal cells (MSC) among other cellular and non-cellular elements, has limited the development of targeted therapeutic alternatives. In this context, hematopoietic cell transplantation (HCT) with autologous cells (i.e. from the patient) has demonstrated to be a feasible and effective therapeutic strategy in severe forms of AA. This strategy is useful to circumvent limitations regarding first-line therapies, especially allogeneic HCT (i.e. with cells from an immuno-matched donor), as well as immunosuppressive (IS) therapy. However, in AA, autologous HCT (auto-HCT) is hampered by the limiting numbers of HSPC collected and by the difficulties posed to ex-vivo expansion of HSPC, especially in those patients that do not achieve a significant hematological response to IS therapy.

STRATEGY

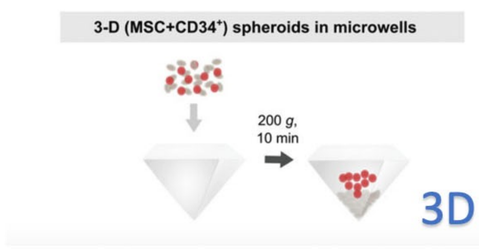
Bone marrow (aa + controls)



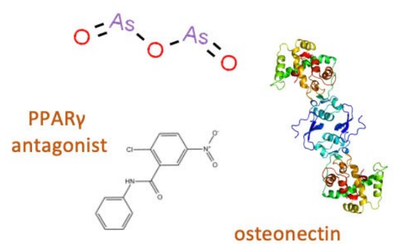
MSCs (aa vs. controls)
- ***Isolation***
- ***Expansion***
- ***Characterization***



MSCs (aa vs. controls)
- Co-culture (HSPCs +/- MSCs differentiated osteoblasts)



Co-culture modulation
- Drugs/small molecules/proteins

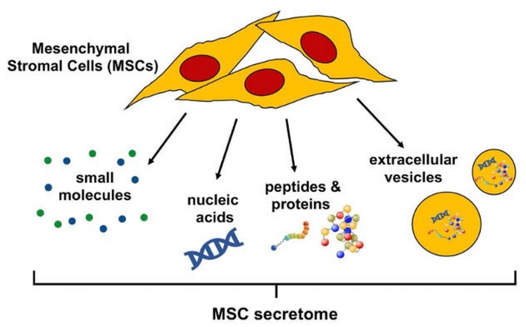


3D platform

- ***Drug screening***
- ***HSPCs (autologous) expansion strategies***
- ***Study drug effect - personalized medicine***

… lab and clinical collaboration

- ***Add complexity to the model (other ME cells – ex. Adipocytes)***
- ***3D scaffold***
- ***Bioreactors***
- ***Develop new MSC based treatment strategies (ex. Secretome)***



regenerative medicine-based therapeutic strategy(s)

GOALS & FUTURE WORKS

The project aims to contribute to improve the feasibility and widen the therapeutic application of auto-HCT as a first-line therapy for AA, namely targeting those patients where allo-HCT is unfeasible (i.e. minorities lacking a suitable HLA-matched donor) and/or do not respond effectively to IS therapies. The main purpose is to to develop a regenerative medicine-based therapeutic strategy for idiopathic AA.

Supervisor: Professor Cláudia Lobato da Silva
Co-Supervisor: Professor Domingos Henrique

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