Subproject 12: Lymphocytes expansion for neoplasia and immune-mediated disorders immunotherapy

Principal Investigator: *Dimas Covas*

Abstract

The translation of experimental immunotherapy for clinical practice requires the development of efficient, rapid, robust and reproducible cell expansion bioprocesses. Since the cells are the product, the cultivation system must minimize the variability in cell population, to ensure the maintenance of the effector functions of the cells, allow harvest and formulation without damaging the cells and incorporate processes to ensure viability during storage, transportation and administration in a safety and cost-effective manner. For this, the cell expansion technology should be ideally closed and disposable, which allows the expansion according to GMP standards. Taking this into consideration this subproject aims at the development of GMP-compliant bioprocesses for expansion of the immunocompetent cells that will be used in preclinical and clinical trials.

Specific Goals

1. *Isolation and characterization subpopulations of human T and NK cells;*
2. *Development of GMP-compliant bioprocesses for large scale expansion of T and NK cells in bioreactors;*
3. *Phenotypical and functional characterization of expanded T cells;*
4. *Phenotypical characterization; gene expression and citokynes production evaluation as well as functional analysis of the expanded NK cells in cytotoxicity assays, flow cytometry and NK degranulation assays;*
5. *Development of cryopreservation protocols for expanded T and NK cells for clinical application;*
6. *Development of protocols for quality control of the expanded cells.*

Implementation schedule

Metas	Semestres											
	1	2	3	4	5	6	7	8	9	10	11	12
1												
2												
3												
4												
5												
6												

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References

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Subprojeto 12: Expansão de linfócitos para imunoterapia de doenças neoplásicas e imunomediadas

Pesquisador Responsável: *Dimas Covas*

Introdução

A translação da imunoterapia experimental para a prática clínica requer o desenvolvimento de bioprocessos de expansão de células eficientes, rápidos, robustos e reprodutíveis. Uma vez que as células são o produto, o sistema de cultivo deve minimizar a variabilidade na população celular, garantir a manutenção das funções efetoras das células, permitir a coleta e formulação sem danificar as células e incorporar processos para garantir a viabilidade durante a estocagem, transporte e administração de maneira segura e com custo reduzido. Para isto, a tecnologia para expansão das células deve estar baseada em sistemas, idealmente fechados e descartáveis, que permitam a expansão de acordo com as normas GMP. Levando isto em consideração este subprojeto tem como objetivo o desenvolvimento de bioprocessos, compatíveis com as normas GMP, para expansão das células imunocompetentes que serão utilizadas nos ensaios pré-clínicos e clínicos.

Metas

1. *Isolar e caracterizar as subpopulações de células T, Tregs e NK humanas;*
2. *Desenvolver bioprocessos em condições compatíveis com as normas GMP para expansão em larga escala de células T, Tregs e NK em biorreatores;*
3. *Caracterizar o imunofenótipo, avaliar a expressão de genes imunorreguladores e avaliar funcionalmente as células Tregs expandidas in vitro em ensaios de supressão de linfócitos in vitro;*
4. *Caracterizar o imunofenótipo, avaliar a expressão de genes relacionados, avaliar a produção de citocinas, e avaliar funcionalmente as células NK expandidas in vitro em ensaios de citotoxicidade por citometria de fluxo e ensaios de degranulação de células NK);*
5. *Desenvolver protocolos de criopreservação das células Tregs e NK humanas expandidas in vitro para aplicação clínica em várias infusões;*
6. *Desenvolver protocolos para o controle de qualidade dos produtos celulares para aplicação clínica.*

Cronograma de execução referente a seis anos de projeto

Metas	Semestres											
	1	2	3	4	5	6	7	8	9	10	11	12
1												
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Referências

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