

MSCNET



A translational programme identifying and targeting the myeloma stem cell

Background

Multiple Myeloma (MM) is a disease where malignant plasma cells accumulate in the bone marrow. Normal and malignant plasma cell development at this site is thought to reflect a synchronous terminal differentiation of B cells that have followed sequential stages of maturation in parallel with a stepwise oncogenesis.

MM is at present an incurable disease, for which effective new therapies are being actively sought. It is by no means clear however what the nature of clonal propagation is in the clinical spectrum of MM. Disease characterization has revealed a number of phenotypic and molecular features that suggest the existence of a clonally-related 'less mature' cell, and the question arises whether this may include Myeloma Stem Cells (MSC) – which are critical to and harbour specific molecular genetic events propagating the malignancy.

To progress work in this area, myeloma researchers from the European Myeloma Network established the myeloma stem cell network (MSCNET), which has set out to identify the nature of the cell underlying disease origin and persistence.

Hypothesis

Our *hypothesis* is that the MSC can be defined and characterized to underpin effective targeted therapy in MM. In this disease, the current state of the art suggests that a preplasmablastic CD19+CD20+CD138- cell may exist as a putative stem cell. However, there is evidence which points to an alternative view, that the MSC may be a CD19-CD20-CD138+ plasmablast/plasma cell. It is conceivable that both or even more stem cell components may be relevant for the oncogene hits responsible for MM progression.

Objectives and aims

It is the *objective* of this project to fully evaluate and significantly extend our current efforts to characterize the stem cell compartments in MM. To this end, our *specific aims* are 1) to develop protocols to identify the potential MSC compartments using overlapping experimental approaches; 2) to isolate and functionally characterize the MSC compartments in different disease subsets of MM; 3) to investigate the mechanisms of MSC persistence and evolution, which gives rise to disease heterogeneity in MM and 4) to define MSC-associated characteristics and antigens for future targeted therapy.

Work performed

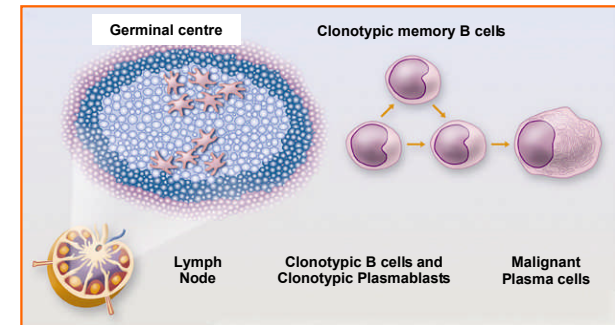
During the second year we have extended the structural network with secure funding to underpin the coordinated research activities and the formulated scientific framework.

We have expanded our home page for communication among partners by establishing a MSCNET FORUM for dissemination and discussion of new data generated and its results.

We have had two scientific network meetings in Copenhagen and Brussels during 2008 and were invited to organize a Scientific Working Group Myeloma meeting during the EHA annual meeting in Copenhagen presenting a programme on The Myeloma Stem Cell.

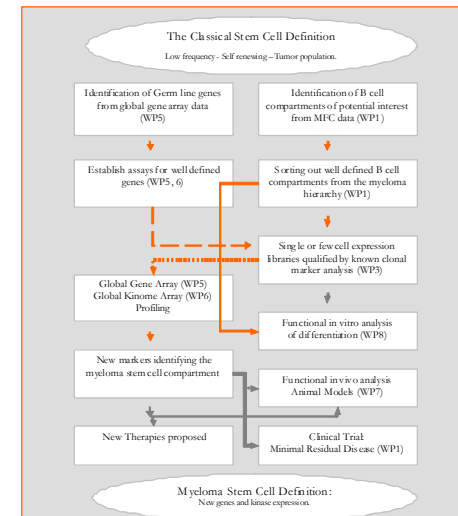
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Thematic Priority: Priority 1, Life Sciences, Genomics and Biotechnology for Health.



There are two routes in the germinal centre leading to the malignant plasma cell clone. Either the MSC is present upstream in the post-germinal clonotypic B cell compartment including memory B-cells and/or plasmablasts, or present within the malignant plasma cell population.

Graphical presentation of work packages and scientific work plan



The diagram shows the progress (by orange arrows) and level of information obtained.