E-Selectin Ligand Expression increases with Progression of Myeloma and Induces Drug Resistance in a Murine Transplant Model, Which is Overcome By the Glycomimetic E-Selectin Antagonist, GMI-1271

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**Multiple Myeloma and E-Selectin**

- Myeloma is an incurable disease of plasma cells that spreads from one to multiple bone sites
- A key feature of MM is the intimate connection and dependency of malignant cells with the bone marrow (BM) microenvironment
- E-selectin regulates the Step-1 rolling interaction required for tissue-specific cell migration and is constitutively expressed in the specialized BM endothelium where it regulates the migration and recruitment of Human Stem/Progenitor cells (HSPCs) to the BM
- Functional E-Selectin ligands are characterised by reactivity with the HECA-452 antibody

**Hypothesis and Methodology**

Given the importance of the BM microenvironment in MM disease and the requirement of E-selectin for homing into the BM niche, the role of E-Selectin and their ligands for the biology of MM were examined

**Objectives**

- Assess the in vitro functionality of E-selectin ligands on Multiple Myeloma cells
- Determine the tumorigenic potential of HECA-452 enriched Multiple Myeloma cells in xenograft mouse models
- Examine the expression of the HECA-452 epitope on Multiple Myeloma primary samples

**Primary Myeloma cells are positive for HECA-452 with high percentage of positive cells in the Peripheral Blood which increases with disease progression**

**Conclusions**

- Multiple Myeloma cells express functional E-Selectin ligands
- HECA-452 positivity tends to be higher in circulating Multiple Myeloma cells of Relapse Patients
- HECA-452 Enriched cells display aggressive disease and resistance to bortezomib in vivo which can be reverted by GMI-1271
- E-selectin ligand bearing cells play an important role in dissemination, disease progression and drug resistance in Myeloma

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