**RESULTS**

M402, a Heparan Sulfate Mimetic, Inhibits Tumor Revascularization and Invasiveness after High-Dose Taxane Treatment in a Mouse Breast Cancer Model

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**BACKGROUND**

Treatment with certain anti-cancer agents, particularly taxanes and sunitinib8, can lead to mobilization of pro-angiogenic factors and subsequently Endothelial Progenitor Cells (EPCs), which home to the viable tumor microenvironment where they participate tumor vascularization. This phenomenon has been linked to rapid tumor regrowth following treatment and may thus diminish its long-term efficacy.9 EPCs as well as other bone-marrow-derived stromal cells are mobilized in response to stimulating pro-angiogenic growth factors and chemokines (VEGF, FGF, G-CSF, IL-6, SDF-1α, etc.) that are induced by certain drugs or in the progressing tumor microenvironment of these tumors. Current heparan sulfate-based approaches to the anti-angiogenic treatment of cancer are mostly based on heparin, a large polymer of sulfated GAGs. Here, we tested a novel heparan sulfate mimetic, M402, for its ability to inhibit:

a) EPC mobilization
b) EPC function on tumor angiogenesis, and
c) Tumor invasiveness and metastasis

d) as a result of interference with matrix.8 Here, we tested a novel heparan sulfate mimetic, M402, for its ability to inhibit:

**MATERIALS / METHODS**

Materials. Docetaxel was purchased from Sanofi-Aventis. Antibodies for fine cytometry and histology were from Biologend, BD Biosciences (CD13, or Biocytin (CD13)). M402 was prepared at Momenta by controlled depolymerization of unfractionated heparin with nitrous acid and then subjected to sequential periodate oxidation and borohydride reduction. The final product was isolated by salt-methanol precipitation to yield a glycol-split heparan sulfate mimic.

**CONCLUSIONS**

- M402 inhibited EPC mobilization in response to docetaxel or 4T1-tumor secreted factors by trapping the EPCs in the bone marrow.
- M402 affected recruitment and outgrowth of EPC/stromal cells in the tumor, leading to reduced tumor vascularization, invasion and metastasis in response to docetaxel.

The experimental data provide a rationale for the clinical investigation of M402 in combination with taxanes or other agents that induce similar effects (such as radiation, 5-FU, cyclophosphamide, sunblitz, etc.).

**ACKNOWLEDGEMENTS / REFERENCES**

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