Using Magnetosome Genes for MRI Reporter Gene Expression

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There is a critical need to noninvasively image molecular activities that define early stages of disease progression. For this, the magnetosome is an ideal structure by which reporter gene expression for molecular, magnetic resonance imaging (MRI) may be refined [1]. We hypothesize that the optimal expression of magnetosome-like nanoparticles in mammalian cells requires a subset of magnetotactic bacterial genes and may be tailored to specific magnetic resonance (MR) signatures that reflect biomineral localization, size, shape and composition.

To improve the formation of magnetosome-like particles for mammalian cell tracking, we are examining genes deemed essential for magnetosome vesicle formation. In bacteria, this step is not only critical to compartmentalizing the iron biomineral and protecting the cell from iron toxicity but may also confer a regulatory role in magnetosome formation [2]. We expressed *mamI*, *mamL, mamB* and *mamE* (from *Magnetospirillum magneticum* species AMB-1) in human MDA-MB-435 melanoma cells, using vectors with fluorescent protein tags. Fluorescence microscopy of the resulting fusion proteins identified sub/cellular location and potential for spontaneous co-localization. For example, MamI expression resulted in the formation of circular structures which co-localized with MamL at the cell periphery (Figure 1). The effect of these magnetosome protein-protein interactions on transverse relaxation rates, measured at 3 Tesla in transfected cells mounted in a gelatin phantom [3], indicated the influence on MR contrast and role of extracellular iron (250 µM $Fe(NO_3)_3$/medium).

In summary, the formation of magnetosome-like particles for mammalian cell tracking may benefit from a subset of magnetotactic bacterial genes as well as clarify the role that individual magnetosome genes play in the regulation of iron biomineralization. This knowledge will instruct the development of MRI reporter gene expression, predicated on the assembly of a rudimentary magnetosome-like particle in response to select molecular activity.

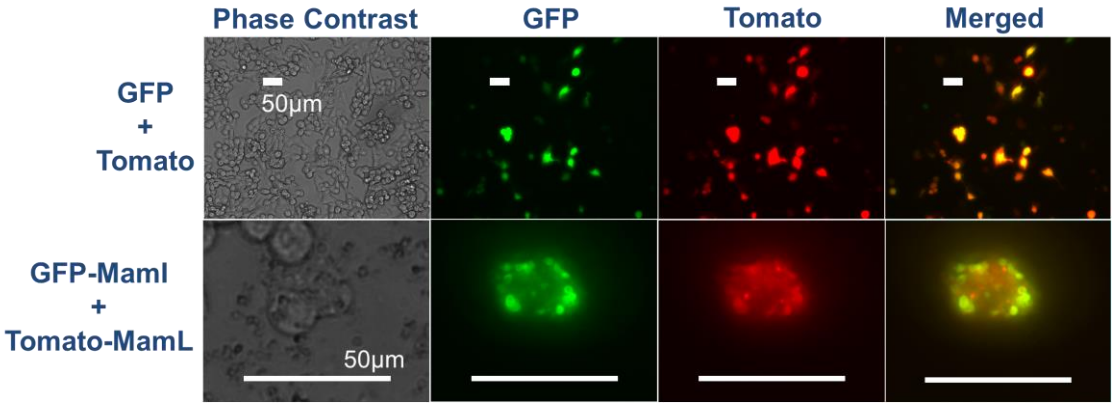

Figure 1. Co-expression of MamI and MamL fusion proteins in MDA-MB-435 cells. GFP-MamI (green) and Tomato-MamL (red) mainly co-localize at the cell periphery in circular structures. Vector images, ~200X; fusion protein images, ~1400X.

References

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