DEVELOPMENT OF HYPERSELECTIVE POLYAMINE TRANSPORT LIGANDS AND SELECTIVITY AGAINST SPECIFIC HUMAN CANCERS. Otto Phanstiel IV, and Aaron Muth, Department of Medical Education, University of Central Florida, 6850 Lake Nona Blvd, Orlando, FL 32827

Polyamine homeostasis is accomplished via a balance of polyamine biosynthesis, degradation, and transport. Rapidly-dividing cancer cells have been shown to have high polyamine transport activity compared to normal cells, likely due to their high requirement for polyamine growth factors. Therefore, the polyamine transport system (PTS) is a therapeutically relevant target as it can provide selective drug delivery to cancer cells. This report describes the synthesis and biological evaluation of new multimeric polyamine derivatives as efficient PTS ligands. A series of arylmethyl-polyamine derivatives were synthesized and evaluated for their ability to target the polyamine transport system. The architectures of these probes addressed two caveats in PTS drug design: a) PTS selectivity and b) metabolic stability to amine oxidases. The optimal PTS-targeting ligand was shown to be approximately 60 times more toxic to MALME-3M (human melanoma) than the matched MALME-3 (normal) cell line.