Carbonic Anhydrase 12 as an Imageable Reporter for Estrogen Receptor and Androgen Receptor Function

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Recent whole genome transcription profiling has revealed many genes under estrogen and androgen regulation; these genes could provide information as to the functionality of the ER or AR signaling system, and therefore, predict the effectiveness of hormone therapy in breast and prostate cancer treatment. Carbonic Anhydrase 12 (CA12) is not only rapidly and highly hormone regulated, but it is also membrane localized and possibly imageable using selective inhibitors. We aim to develop membrane-impermeable compounds by tethering known CA12-specific inhibitors to nanoparticles or dendrimers which will restrict the inhibitor to extracellular targets. A fluorescence polarization assay using the soluble extracellular domain of CA12 and a fluorescein-labeled inhibitor has been used to test the binding affinities of different CA12 inhibitors before and after tethering to these particles. Studies with several fluorophore-labeled CA12 inhibitors in MCF7 cell culture studies have shown the upregulation of CA12 and the specificity with which these inhibitors bind to the targeted isozymes. In this manner, we anticipate using imaging techniques to monitor changes in the levels of CA12 that result from hormone treatment of breast and prostate cancer patients and acquiring information to predict outcomes of endocrine therapy.