Laurie Parker, PhD: Synthetic organic chemistry, advisor David Robins, University of Glasgow, UK (2000-2003). Postdoc: Proteomics and chemical biology, advisors Stephen Kent and Stephen Kron, University of Chicago (2003-2008). Our research program is broadly directed at assay development for post-translational modifications (PTMs), with a focus on protein phosphorylation. We use a “decoy” substrate biosensor approach in which an artificial, optimized substrate peptide is designed to report the activity of a specific enzyme in living cells. Substrates are designed using preference motifs derived from in-house phosphoproteomics experiments. Substrate delivery is achieved using cell-penetrating peptides, and enzymatic modification is measured using a range of readout strategies—some that require extraction of the cell contents and some that leave the cell intact. Targeting the function of the enzyme in its intracellular environment preserves protein-protein interactions, localization, and scaffolding-dependent activation, and decoy substrates provide a snapshot of enzymatic activity that circumvents the need for pre-knowledge of every endogenous substrate site. We also develop multiplex-compatible readouts via proteomics and imaging strategies, so we can use a suite of biosensors for different enzymes in order to profile pathways.