

## **A Cell-Based High-Throughput Screen Assay for Positive Modulators of Insulin Receptor**

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Compounds that mimic insulin could form the basis for an orally available treatment of type II diabetes. As with other growth factor receptor tyrosine kinases (GF-RTKs), the insulin receptor (IR) is autophosphorylated at tyrosine residues upon insulin binding. To date, cellular methods that measure the phosphorylation of GF-RTKs incorporate at least one wash step and are thus not ideal for HTS. Here we describe a homogeneous cell-based assay that uses the MesoScale Discovery (MSD) technology platform and allows rapid, robust and sensitive measurements of IR phosphorylation. The assay has the advantage of being practical (cells are added as a suspension), homogeneous (no wash steps, despite being a sandwich immunoassay) and versatile (it can detect both insulin mimetics and inducers). The HTS has been completed against the entire GSK collection returning average values of  $z'=0.64$ , Signal/Background=5.3 and  $pEC50=9.18\pm 0.14$  for the insulin standard.

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