

O-33: PROBING EXTRACT AND PURE NATURAL PRODUCT COMPOUND LIBRARIES FOR INHIBITORS OF HIF-2 INDUCED GENE TRANSCRIPTION

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A multiphase high throughput screening (HTS) assay has been developed for the identification of inhibitors, from natural products sources, of HIF-2 induced gene transcription. This was achieved through the engineering of luciferase reporter cell lines where reporter expression was modulated by the interaction of the HIF-2 transcriptional activation complex with the hypoxia response elements of either the vascular endothelial growth factor or the human endothelial nitric oxide synthase genes in the stably transfected clear cell renal carcinoma cell line 786-O. Evaluation of compatibility of reporter readout with exposure to extracts from different sources revealed that the assay was compatible with such treatment with no further need for a wash step before reporter readout. To date, a library of about 5000 pure natural product-derived compounds and 140,000 extracts have been screened using this HTS assay. The compounds and extracts were obtained from NCI's collection of plants, marine organisms and microbes.