CETSA® HT: A new publication highlights its unique capabilities.

The Cellular Thermal Shift Assay (CETSA) developed by Pelago Bioscience enables the direct detection of compound binding to the drug target within cells. A strategic collaboration was established between Pelago Biosciences and AstraZeneca in 2015 to apply this method to the study of drug action across projects within the AstraZeneca discovery portfolio. The first scientific manuscript arising from this collaboration has been published in Nature Scientific Reports that demonstrates the creation of a novel CETSA® HT assay that can exclusively identify compounds that directly bind to the human Androgen Receptor and is capable of differentiating such direct binders from co-regulator inhibitors that other cellular assays measuring functional responses cannot.

The identification of novel Androgen Receptor (AR) antagonists has been made challenging by the lack of disease relevant cellular methodologies capable of discriminating between inhibitors that directly bind AR and those that instead act on AR co-regulators. Steve Rees, Vice President of Discovery Biology at AZ commented: '*The work described in the Nature Scientific Reports publication enables the identification of novel drugs that inhibit the activity of the human Androgen Receptor and further demonstrates the quality of the collaboration between AstraZeneca and Pelago*.'

The authors were also able to use the displacement of an AR agonist by test compounds to derive intracellular binding affinities of antagonists. These results of quantifying antagonist-receptor Ki values in a label free and disease relevant context is a first and holds promise for the discovery of novel therapies targeting AR.

Pelago Bioscience CSO Daniel Martinez Molina is enthusiastic about this joint publication establishing the value of CETSA® in early discovery for screening and hit confirmation. *'With CETSA® HT it is possible to identify direct binders of your target in a cellular context. The plate based format allows for high throughput testing of large compound libraries to identify novel chemistry for previously intractable targets.'*

Determining direct binders of the Androgen Receptor using a high-throughput Cellular Thermal Shift Assay.
Shaw J, Leveridge M, Norling C, Karén J, Molina DM, O'Neill D, Dowling JE, Davey P, Cowan S, Dabrowski M, Main M, Gianni D.
Nature, Scientific REPORTS (2018) 8:163

Read the full publication here: http://rdcu.be/Enrl

About Pelago Bioscience AB

Spun out from the Karolinska Institute, Stockholm Sweden, Pelago Bioscience AB (http://pelagobio.com) was founded to provide and develop the patented Cellular Thermal Shift Assay (CETSA®) for use in determination and quantification of drug–target interactions. The company delivers *in situ* target engagement studies to accelerate preclinical and clinical drug discovery and diagnostics development. Using CETSA data and applications, drug discovery R&D companies are able to make better and more informed decisions at earlier stages in their projects. This reduces time and money spent on the non-optimal compounds and allows faster development of more efficacious new drugs.