

## Our new premises at The BioHub Birmingham

Taking advantage of a substantial EU grant, we have relocated to a purpose-built facility, fitted out with a full array of standard and specialist equipment. "The laboratory is exceptionally well equipped with new and top-of-the line equipment. Freezers (-152 °C, -80 °C), liquid nitrogen, tissue culture, flow cytometer, HPLC, cryostat, scintillation counter, balances, centrifuges... With these premier facilities, Gifford Bioscience will continue to excel in providing only the highest quality radiometric assays." Dr Andrew Gifford, Chief Scientific Officer.



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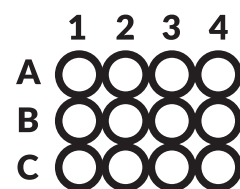
Gifford Bioscience is a preclinical contract research organization (CRO) providing pharmacology services in receptor occupancy, radioligand binding assays, cell-based assays and autoradiography.

The company was originally founded (2008) as InvivoPharm Inc, a CRO based on receptor pharmacology and occupancy.

We are a specialised company, using “gold standard” radiometric techniques in our assays. This ensures high sensitivity and robustness in all our studies.

In addition to undertaking standard or custom assays on a client’s sample to our client’s specification, our capabilities include assay design, in-house production of membrane preparations, cell culture facilities and, through our connection with the University of Birmingham, animal dosing and assays requiring human tissue samples.

In 2017, we relocated to The BioHub Birmingham, a cluster of life sciences businesses based at the University of Birmingham’s research park.



### Radioligand binding assays

Radioligand binding assays enable rapid and cost-efficient determination of compound affinities, receptor density and kinetic parameters for receptor-ligand interactions in cells and tissues. Assay protocols can be competition, saturation or kinetic.

#### Competition binding assays

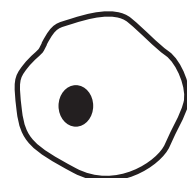
- Determination of  $IC_{50}$  and  $K_i$  values for test compounds against a membrane receptor.
- Membrane receptor preparations obtained from cells or tissues.
- Assays are robust and reproducible compared with less direct alternatives.

#### Saturation binding assays

- Yields both affinity ( $K_d$ ) and density ( $B_{max}$ ) for receptor-ligand interactions for membrane receptors.
- Identification of competitive versus non-competitive (allosteric) mechanisms for binding interactions.
- Determination of occupancy versus concentration relationships for radiolabeled proteins or antibodies to cell surface receptors in cell culture.

#### Kinetic binding assays

- Association ( $k_{on}$ ) and dissociation ( $k_{off}$ ) rates.
- Identification of allosteric effects on ligand dissociation.



### Cellular uptake and release assays

Radiometric uptake and release assays are used to quantify the potency and efficacy of test compounds on cellular uptake processes, neurotransmitter release or ion channel activity.

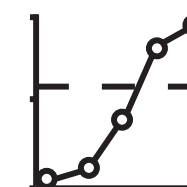
- Determination of  $IC_{50}$  and  $K_i$  values for test compounds against cellular or synaptosomal uptake of tritiated neurotransmitters and metabolites.
- Quantification of drug effects on ligand-gated ion channel activity via  $^{86}Rb$  efflux.
- Quantification of cell-mediated cytotoxicity via  $^{51}Cr$  release.



### Receptor autoradiography

Receptor autoradiography enables the distribution and density of receptors for a labeled ligand to be determined in tissue sections.

- Effect of chronic drug treatments on receptor density and affinity across brain or tissue regions.
- Determination of agonist efficacy on GPCRs via [ $^{35}S$ ]GTP $\gamma$ S binding.
- Visualization of known and unknown binding sites for a labeled ligand in tissues.

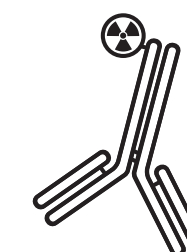


### Receptor Occupancy

Receptor occupancy assays measure the percentage to which a test drug occupancies its target receptor in brain or peripheral tissues. Occupancy is determined by measuring competition with binding of a radiolabeled tracer to the receptor.

#### Ex vivo/In vivo receptor occupancy

- Central receptor occupancy estimation over a range of drug doses or time points.
- Establish pharmacokinetic and pharmacodynamic relationships of a drug candidate.
- *Ex vivo* autoradiographic determination of receptor occupancy in different brain regions or across multiple receptors.



### Radiolabeling services

#### Radioiodination

Labeling of proteins, antibodies and peptides with radioiodine ( $^{125}I$ ,  $^{131}I$ ) for use in our *in vitro* and *ex vivo* receptor binding studies.

#### Tritiation

Tritium labeling of small molecules using *O* or *N*-methylation with tritiated methyl iodide. A suitable precursor needs to be supplied by the client.