

# **gifford** BIOSCIENCE LIMITED



[www.giffordbioscience.com](http://www.giffordbioscience.com)

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

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

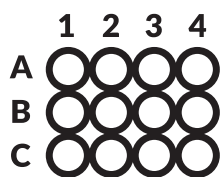
Our radioactive substances permit encompasses all common laboratory radioisotopes: Tritium; Iodine-125; Iodine-124; Iodine-131; Carbon-14; Sulphur-35; Phosphorus-32; Phosphorus-33; Chromium-51; Rubidium-86 and smaller amounts of other beta/gamma emitting radionuclides.

We undertake standard or custom assays, either to our client’s existing specification or after a discussion over assay design.

Supporting capabilities include:

- cell culture
- in-house production of membrane preparations
- assays requiring human tissue samples (working with the University of Birmingham Human Tissue Bank and the UK Brain Bank Network)
- assays requiring animal tissue (*in vivo* or *ex vivo*)





## 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

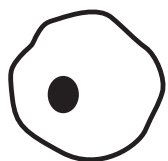
- Determination of  $IC_{50}$  and  $K_i$  values for test compounds against a membrane receptor and other target types.
- Membrane receptor preparations obtained from cells or tissues.
- Assays are robust and reproducible compared with less direct alternatives.

### 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.

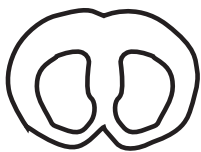


## Cellular uptake and release assays

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  $IC_{50}$  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.

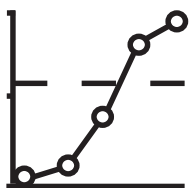




## Receptor autoradiography

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

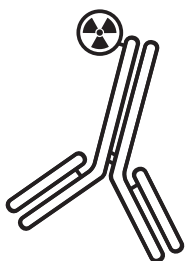
- Measurement of receptor density in specific brain regions.
- Visualization of known and unknown binding sites for a labelled ligand in tissues.
- Effect of chronic drug treatments on receptor density and affinity across brain or tissue regions.
- Determination of agonist efficacy on GPCRs via [<sup>35</sup>S]GTPγS binding.



## Receptor occupancy

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

- 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 (<sup>125</sup>I, <sup>131</sup>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. For other tritiation approaches, we work with specialist partner companies.



# Our premises at The BioHub Birmingham

Gifford Bioscience Limited is located at a purpose-built facility on the University of Birmingham's Research park. The laboratory is fitted out with the full array of standard and specialist equipment to meet our needs: liquid nitrogen; remotely monitored freezers at  $-152\text{ }^{\circ}\text{C}$  and  $-80\text{ }^{\circ}\text{C}$  as well as  $-25\text{ }^{\circ}\text{C}$ ; dedicated tissue culture room; cryostat; liquid scintillation counter; HPLC; flow cytometer; brightfield and fluorescence microscopy. The facility was opened in 2015, having been funded through a substantial EU grant.



[www.giffordbioscience.com](http://www.giffordbioscience.com)



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