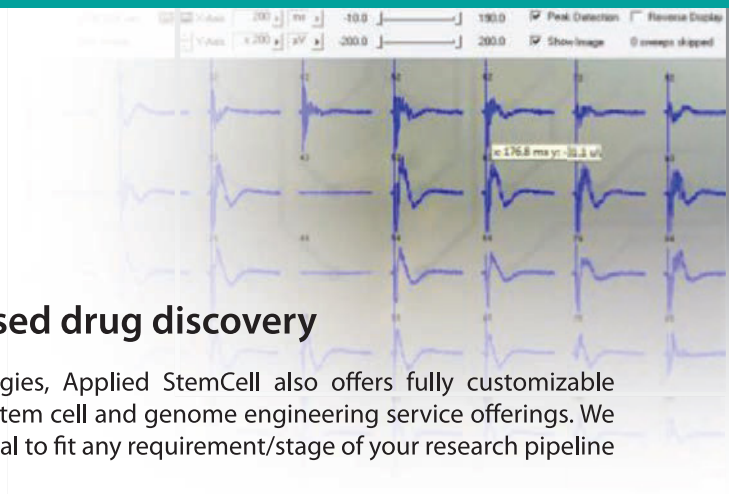


Applied StemCell

Genome editing *in vitro* and *in vivo*

Custom *In Vivo* Assay Services

Fully customizable assay platform for *in vivo*-based drug discovery

As a long-standing leader in genome editing and stem cell technologies, Applied StemCell also offers fully customizable downstream animal service solutions that goes far beyond our standard stem cell and genome engineering service offerings. We can meet the unique needs of our clients by customizing projects piecemeal to fit any requirement/stage of your research pipeline such as:

- Designing and engineering research animal disease models
- Adoptive transfers/transplantation
- *In vivo* behavioral analyses
- Functional screening using electrophysiology, EEG & EMG
- Drug efficacy & toxicity screening

Areas of Application:

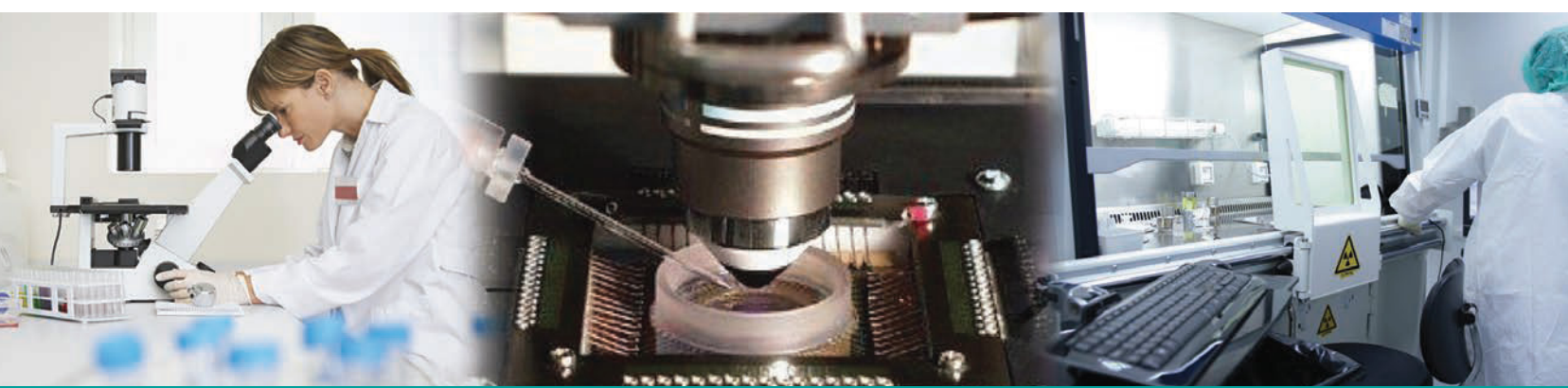
- Cancer & immunotherapies
- Neurological diseases
- Reproductive & developmental biology
- Drug screening

Below is a selected list of assays available for your *in vivo* assessments:

1. Disease Model Generation	• Genetically modified mouse and rat models • Adoptive cell transfer, teratomas • Surgically/drug induced models
2. *In Vivo* Assays	• Behavioral assessments: cognition & locomotor activity • Automated *in vivo* measurements: ECG, EEG, EMG • *In vivo* pharmacokinetics
3. *In Vitro*/Postmortem Assays	• Electrophysiology: neurological & cardiac assays; patch-clamp, MEA • Tissue collection and end-of-study analyses: western blots, immunohistochemistry, RT-PCR

Why choose ASC's custom *in vivo* services?

- NIH Office of Laboratory Animal Welfare (OLAW) Assurance
- DEA licenses: Schedule I & Schedule II-V
- State-of-the-art vivarium with automated behavorial assessment cages & devices
- Multidisciplianry team of experts to design a comprehensive project plan
- Stress-free projects with dedicated project managers



Electrophysiology Assays for Disease Modeling, Drug Discovery and Drug Screening

Examples:

1. Cardiac Ion Channel Safety Screening Using Manual Patch Recording

Screening for potential cardiotoxicity of novel drug candidates that modulate key ion channels. Utilizing our expertise in patch-clamp electrophysiology, drugs can be screened against an array of ion channels including recombinant human ether-a-go-go deleted gene (hERG), Nav1.5, Cav1.2, and using human iPSC-derived cardiomyocytes.

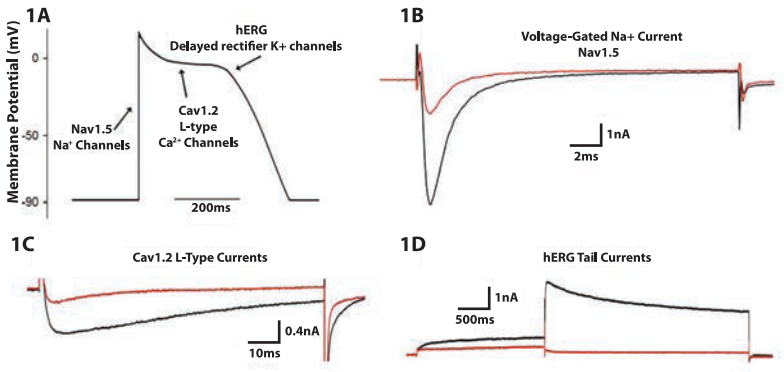


Figure 1. Several ion channels involved in the cardiac action potential are implicated in QT interval prolongation. (B-D) Example recordings showing drug inhibition of human Nav1.5, Cav1.2 and hERG currents. Black traces represent control currents and red traces show currents in the presence of representative inhibitory drugs.

2. Functional Screening Assays to Test Neurological Endpoints Using Patch Clamp Recording

Electrophysiological recordings in rodent brain slices for disease model validation and drug efficacy/safety. Standard electrophysiological recordings of acutely prepared brain slices are used to measure changes in membrane potential, cell excitability, spike firing, and synaptic neurotransmission, including long-term potentiation/ depression (LTP/LTD).

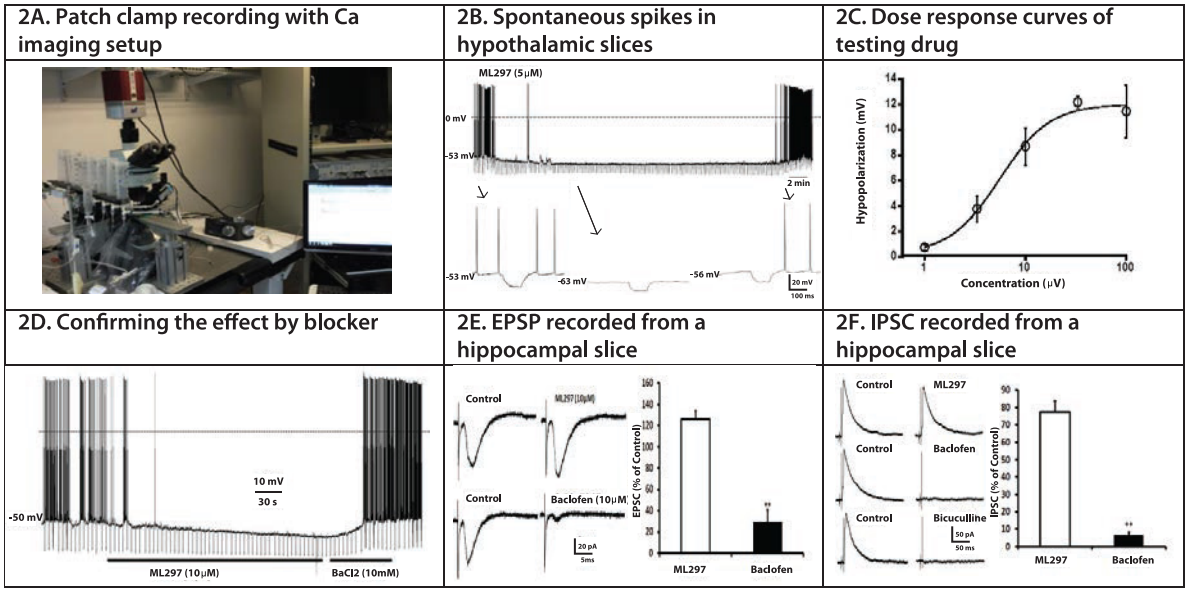


Figure 2. Mice were euthanized and the brains were quickly isolated and placed into ice-cold artificial cerebrospinal fluid (ACSF), continuously bubbled with 5% CO_2/95% O_2. The ACSF is composed of (in mM) NaCl 124.0, KCl 2.5, KH_2PO_4 1.2, $CaCl_2$ 2.4, $MgSO_4$ 1.3, $NaHCO_3$ 26.0 and glucose 10.0 (pH 7.4). Slices (260 μm thick) containing hippocampus and/or thalamus were prepared using a vibratome (Leica), and incubated at room temperature in continuously oxygenated ACSF for at least 1 h before recordings at room temperature. Slices were continuously perfused with ACSF bubbled with 5% CO_2/95% O_2 at a flow rate of 1 mL/min from an elevated reservoir. Recordings were made using an Axon 700B patch clamp amplifier, Axonpatch 1D for extracellular recordings, or a 64-channel multi-electrode array (MEA-64, Multi-Channel Systems).

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