For Any Technical Questions, Please Contact at info@nodesus.com

Product Name: Ion Channel Reader

Part Number:

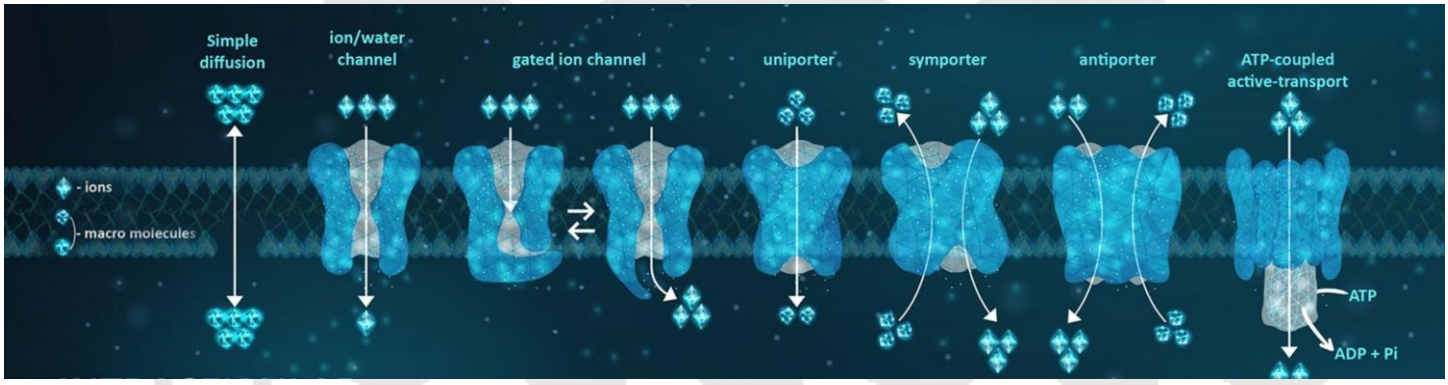
Product Description:

Ion Channel Reader :

Ion Channel & Transporter Screening Technology

Human genome sequencing identified more than 400 alleged ion channels and transporters. only limited numbers of these membrane proteins are functionally tested. The extensive tissue distribution of ion channels and transporters and their physiological functions made these proteins important therapeutic targets in drug discovery, development, and safety. Besides, these membrane proteins are expressed in different types of human cancers and represent novel cancer biomarkers. Ion channels are also expressed in the new SARS-CoV-2 virus and on the membrane of its host cells and are considered potential drug and vaccine development targets for COVID-19. With the advent of new technologies in ion channel screening, our knowledge is significantly strengthened. Aurora Biomed's Ion Channel Readers (ICRs) combine the versatility, precision, and sensitivity of atomic absorption spectroscopy (AAS) with the microsampling process and liquid handling technologies, creating a mid to high-throughput screening solution for ion channel researchers that fills gaps, which automated patch-clamp cannot.

Different Types of Ion Channels & Transporters



Aurora's Ion Channel Reader Series (ICR series) combine atomic absorption spectroscopy (AAS) with a patented microsampling technology to accurately measure ion movement in a cell-based assay format. This technology has been developed with the capability of measuring activity of voltage-gated and ligand-gated ion channels, co-transporters and pumps. It is considered as an effective and high throughput solution to investigate a broad range of membrane proteins including electroneutral targets, to which conventional electrophysiology cannot be applied.

The ICR series detect ion movements across membrane proteins through quantifying intracellular and extracellular ion concentrations of interest using AAS. This is a technique that is independent of, and complementary to methods that rely on voltage manipulation. Since ion flux is a direct measure of channel activity, such assays are robust and less sensitive to disturbances, and data generated by the ICR Series are very consistent and predictive of drug potency.

Therefore, ICR can be used as a primary screening application for ion channel drug research and

development, or as a secondary screen for drug safety evaluation.

ICR8100 is suitable for medium throughput screening, 3-4 samples can be analyzed per minute and 96/384 well plates can be used as sample containers. At the same time, the highly sensitive ICR8100 can detect as low as 0.05 ppm Rb+. Even if the detection dosage is as low as 50 uL, the detection sensitivity of ICR8100 is maintained.

ICR12000 is suitable for high throughput drug library screening and processing requirements of ion channel targets. The processing capacity is 12 times that of ICR8100. The instrument is fully automated, equipped with a stacker and barcode scanner. At present, it is Aurora's highest throughput instrument- handling up to 60,000 sample wells per day.

ICR 8000

ICR 12000

Applications:

Ion Channel Types	Related Diseases	Application Report Publication
ERG	Long QT Interval Syndrome, Drug-induced Arrhythmia	Merck, Athersys Inc., Schering-Plough
KCNA3(Kv 1.3)	Sclerosis	Merck

KCNQ2/3	Epilepsy	Wyeth, AstraZeneca
KCNA5(Kv 1.5)	Pulmonary Hypertension	Merck
BK_{Ca}, SK_{Ca}	Erectile Dysfunction, Incontinence	Abbott
KCNA4(Kv 1.4)	Ventricular Diseases	
KCNA1(Kv 1.1)	Episodic Ataxia	
Na^+/K^+-ATPase	Congestive Heart Failure	Aurora
K-Cl co-transporter		
K-ATP		BC
$Na_v1.7$	Pain	AstraZeneca
$Na_v1.5$	Long QT Interval Syndrome	AstraZeneca
$Na_v1.2$	Sclerosis, Spasm	
CFTR	Cystic Fibrosis	
	Asthma	Aurora,Hebei Medical University
Stretch-activated K^+	Muscle/Cardiomyocyte Injury	Aurora

Feature:

ICR 8100

Product Characteristics

√Medium Throughput: Up to 5000 samples per day
√Single Channel: Measure a single sample at a time
√Minimum Sample Volume: 50µl
√Sample Container: 96 or 384 well plate
√Size: H.67cm X W.55cm X D.37cm
√Gas: Air Acetylene
√Optional Accessories: Sample Rack, Barcode Scanner
√Sensitivity: Detection Limit is 0.05 ppm
√Accuracy: < 5% CV

ICR 12000

Product Characteristics

√High Throughput: Up to 60,000 samples per day
√Multichannel: Simultaneous measures 12 samples
√Minimum Sample Volume: 20µl
√Sample Container: 96 or 384 well plate
√Size: H.135cm X W.134cm X D.97cm
√Gas: Air and Natural Gas
√Including: Sample Rack, Barcode Scanner
√Sensitivity: Detection Limit is 0.05 ppm
√Accuracy: < 5% CV

ICR 8100 Feature and Benefits

- Programmable and automated solution for up to 5000 wells/day
- Automatic dilution, calibration and cleaning
- Adaptable to existing robotic automation
- Sample dilution not required
- High sensitivity
- On-line dilution
- Eliminates quenching effects associated with fluorescence
- Removes need to work with hazardous radioisotopes
- Avoids work restrictions posed by Rb's short half-life
- Ideal for hERG channel assays
- Can assess both electrogenic and electroneutral transporters

ICR 12000 Feature and Benefits

- Programmable and automated solution for up to 60,000 wells/day
- Automatic dilution, calibration and cleaning
- Integrated plate stacker & bar code reader
- Sample dilution not required
- High sensitivity
- On-line dilution
- Eliminates quenching effects associated with fluorescence
- Removes need to work with hazardous radioisotopes
- Avoids work restrictions posed by Rb's short half-life
- Ideal for hERG channel assays
- Can assess both electrogenic and electroneutral transporters

Product Specification

ICR 8100:

- Medium Throughput: Up to 5000 wells/day
- Single Channel: Measures 1 sample at a time
- Minimum sample volume: 50 µl
- Accommodation: 96/384-well microplates
- Footprint: H.67 cm X W.55 cm X D.37 cm
- Fuel Source: Acetylene / Compressed Air
- Options: Plate Stacker / Barcode Reader
- Sensitivity: 0.05 ppm detection limit
- Precision: < 5% CV

ICR 12000:

- Medium Throughput: Up to 60,000 wells/day
- 12 Channel: Measures 12 sample at a time
- Minimum sample volume: 20 µl
- Accommodation: 96/384-well microplates
- Footprint: H.120 cm X W.95 cm X D.37 cm
- Fuel Source: Acetylene / Compressed Air
- Options: Plate Stacker / Barcode Reader
- Sensitivity: 0.05 ppm detection limit
- Precision: < 5% CV

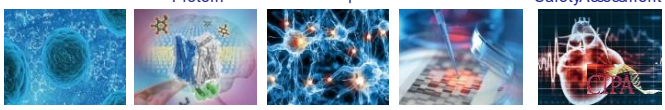
ICR Series
Ion Channel Reader Series

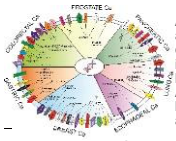
High Throughput, Cost Effective, Automatic

Aurora's Ion Channel Reader Series (ICR series) combine atomic absorption spectroscopy (AAS) with a patented microsampling technology to accurately measure ion movement in a cell-based assay format. This technology has been developed with the capability of measuring activity of voltage-gated and ligand-gated ion channels, co-transporters and pumps. It is considered as an effective and high throughput solution to investigate a broad range of membrane proteins including electroneutral targets, to which conventional electrophysiology cannot be applied.

The ICR series detect ion movements across membrane proteins through quantifying intracellular and extracellular ion concentrations of interest using AAS. This is a technique that is independent of, and complementary to methods that rely on voltage manipulation. Since ion flux is a direct measure of channel activity, such assays are robust and less sensitive to disturbances, and data generated by the ICR Series are very consistent and predictive of drug potency. Therefore, ICR can be used as a primary screening application for ion channel drug research and development, or as a secondary screen for drug safety evaluation.

Stem Cell Research | Ion Transporter Protein | Drug Research and Development | Tumor Markers | Cardiovascular Safety Assessment

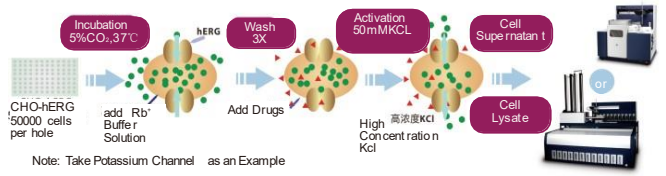




According to the University of Florence research, ion channels and transporters are not only involved in the proliferation, differentiation and apoptosis of cancer cells, but can also be used as tumor markers to some extent. For example, some ion channels and transporters are significantly up-regulated in cancer cell lines but are low or not expressed in the corresponding normal tissues of tumor origin. At present, similar findings have been found in breast cancer, prostate cancer, lung cancer, rectal cancer, esophageal cancer, pancreatic cancer, gastric cancer and other cancer research fields.

With the increase of drug-resistance and drug-induced diseases, the trend of returning to nature is globally prevalent. The research and development of effective components and targets for natural drugs has become a hot spot. For example, in China, the first non-surgical treatment of lumbago and leg pain is a sea snake venom tincture. The tincture utilizes the powerful analgesic effect of the purified sea snake venom peptide and the targets of this mechanism are ion channel receptors on nerve cells. Therefore, there is a rapid growth of interest in these peptide toxins as they contain natural compounds which achieve analgesia, anesthesia and can even help combat drug addiction.

Principle of ICR in High Throughput Screening of Ion Channel Blockers



Note: Take Potassium Channel as an Example

ICR 8100 & 12000

ICR8100 is suitable for medium throughput screening, 3-4 samples can be analyzed per minute and 96/384 well plates can be used as sample containers. At the same time, the highly sensitive ICR8100 can detect as low as 0.05 ppm Rb+. Even if the detection dosage is as low as 50 uL, the detection sensitivity of ICR8100 is maintained.

ICR12000 is suitable for high throughput drug library screening and processing requirements of ion channel targets. The processing capacity is 12 times that of ICR8100. The instrument is fully automated, equipped with a stacker and barcode scanner. At present, it is Aurora's highest throughput instrument - handling up to 60,000 sample wells per day.

ICR8100

ICR 12000

Product Characteristics

√Medium Throughput: Up to 5000 samples per day
√Single Channel: Measure a single sample at a time
√Minimum Sample Volume: 50μl
√Sample Container: 96 or 384 well plate
√Size: H.67cm X W.55cm X D.37cm
√Gas: Air Acetylene
√Optional Accessories: Sample Rack, Barcode Scanner
√Sensitivity: Detection Limit is 0.05 ppm
√Accuracy: < 5% CV

Product Characteristics

√High Throughput: Up to 60,000 samples per day
√Multichannel: Simultaneous measures 12 samples
√Minimum Sample Volume: 20μl
√Sample Container: 96 or 384 well plate
√Size: H.135cm X W.134cm X D.97cm
√Gas: Air and Natural Gas
√Including: Sample Rack, Barcode Scanner
√Sensitivity: Detection Limit is 0.05 ppm
√Accuracy: < 5% CV

Technological Superiority

√ Programming and Automation
√Automatic Dilution, Calibration and Cleaning
√Precise Three-Dimensional Control of Mechanical Automation
√High Sensitivity Detection, Automatic Online Dilution Function
√Avoid false positive / negative with Fluorescence Methods
√Uses Non-Radioactive Tracer Ion Method to Avoid Half-life of Radioactive Substances
√Limit Hands-on Work and Injury to Operators
√Patent Technology Protection: Flame Atomizer Microinjection, Sodium Ion Channel Assay (image of patents to the right)
√Can be used for ion transporters

ICR Technology and Other Research Methods

There are several alternative methods widely available for assessment of ion channel activity. However, only the ICR series can deliver unparalleled speed, precision and reproducibility.

Method	Information Content	throughput	Sensitivity	Accuracy	Comment
ICR8100	Medium	Medium	High	Medium	Applicable to K^+, Na^+, Cl^-, Ca^{2+} channels and transporters
ICR12000	Medium	High	High	Medium	Same as ICR8100
Automatic Patch Clamp	High	Secondary	High	High	Not amenable to electro-neutral targets
Binding Assays	Low	High	Medium	Low	Requires radio-labeled probe specific for target
Radioactive Flux Assays	Medium	Medium	Medium	Medium	Short half-life and exposure concerns
Fluorescent Imaging	Low	High	Medium	Low	Prone to dye artifacts, high cost of consumables & high background noise

Ion Current Precipitation Analysis Flux Assays

Using non-radioactive assay as a screening tool of membrane protein modulators is well-documented in scientific literature and has been widely used for studying the potassium channel family. It is designed and developed to circumvent problems associated with the short-half life and high-energy emission of radioactive 86Rb, while maintaining the information content and accuracy of the radioactive method. Rubidium is so far the most commonly used tracer ion to study potassium channels because of its similar physical properties to K^+, little natural presence in physiological systems, and ease to detect by AAS. The principle of the non-radioactive Rb assay can be easily applied to other membrane protein targets as well.

The application of flux assay is not limited to studying potassium channel activities. Other tracer ions including Ag^+, Li^+, Ca^{2+} and potentially more can be used to screen against different targets in a flux assay format on the ICR series.

Tracer Ion	Ion Channel Types
Rb^+	Potassium Channels and Transporters: hERG, KCNQ2, Kv1.1, Kv1.3, Kv1.4, Kv1.5, Kir6.2, B/SKCa, Slack, KATP, NKCC1, Na/K-ATPase etc.
Ag^+	Chloride Channels and Transporters: KCC2, TMEM16A, CFTR etc.
Li^+	Sodium Channels: Nav1.2, Nav1.5, Nav1.7 etc.
Ca^{2+}/Sr^{2+}	Calcium Channels: Cardiac L-type and more

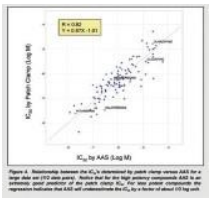
Application Area

Ion Channel Types	Related Diseases	Application Report/Publication (User/Manufacturer)
hERG	Long QT Interval Syndrome, Drug-induced Arrhythmia	Merck, Athersys Inc., Schering-Plough
KCNA3(Kv1.3)	Sclerosis	Merck
KCNQ2/3	Epilepsy	Wyeth, AstraZeneca
KCNA5(Kv1.5)	Pulmonary Hypertension	Merck
BK_{Ca}, SK_{Ca}	Erectile Dysfunction, Incontinence	Abbott
KCNA4(Kv1.4)	Ventricular Diseases	
KCNA1(Kv1.1)	Episodic Ataxia	
Na^+/K^+-ATPase	Congestive Heart Failure	Aurora
K-Cl co-transporter		
K-ATP		UBC
$Na_v1.7$	Pain	AstraZeneca
$Na_v1.5$	Long QT Interval Syndrome	AstraZeneca
$Na_v1.2$	Sclerosis, Spasm	
CFTR	Cystic Fibrosis	
Cl_{Ca}	Asthma	Aurora, Hebei Medical University
Stretch-activated K^+	Muscle/Cardiomyocyte Injury	Aurora

For more applications, please contact Aurora

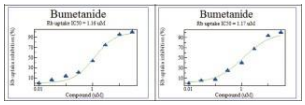
ICR Technology and Patch Clamp Technology

Comparison of Patch Clamp and ICR in Evaluating the Efficacy of hERG Blockers

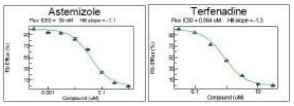


Lundbeck, an internationally renowned pharmaceutical company, uses ICR8000. When testing the results of Rb+ ion current, ICR technology proves to be a reliable and accurate test method, which can reflect the ability of the tested drugs to inhibit the hERG ion channel. The experimental results show that in comparison with patch clamp technology, ion channel technology has a high correlation for verifying drug safety. At the same time, ion channel technology has some essential advantages of low cost, higher throughput and good reproducibility.

Determination of ICR8000 & ICR12000 Blocking Effect of Bumetanil on Cation-Chloride Co-transporter in Nervous System



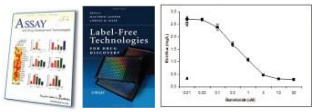
Measurement of Ion Current Blocking Efficacy of Asmidazole and Terfenadine



For Any Technical Questions, Please Contact at info@nodesus.com

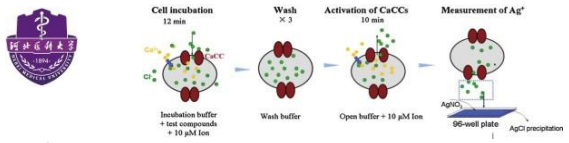
Application Methods

Screening of NKCC1 Cotransporter Targets



Roche Innovation Centre Basel utilize the ICR12000 with the Rb+ flux assay to screen a full library of modulators against a cation-chloride co-transporter. ICR8000 and ICR1200 screening technologies and their applications (▲), and negative controls with absence (△) and are discussed in the literature called, Label-Free Technologies for Drug Screening.

Concentration-dependant inhibitory effect of bumetanide on NKCC1 Rb+ influx activated for 2 min (■), with positive control of 30μM presence of 1 μM of digoxin (□).



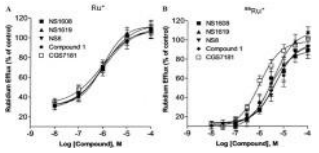
Using Ag^+ as Tracer Ion to Study Modulators of Cl^- Channels

AAS-based detection system for high throughput screening of CaCC modulators. Cl^- flux from CHO cells transfected with TMEM16A is assayed directly by measuring excess Ag^+ ions in the supernatant of AgCl precipitate. The assay can be easily extended to study modulators of other Cl^- channel subtypes.

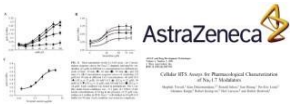
Functional Analysis of Large Conductance Ca^{2+} Activated K^+ Channel

Abbott

The pharmacological profiles of BK(Ca) channels assessed by AAS (A) compare well with those obtained using the Rb+ efflux assay (B). ICR non-radioactive Rb+ method was more suitable for high-throughput screening of new potassium channel regulators.

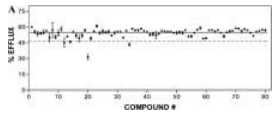


Screening of KCNQ2 Potassium Channel Modulators



AstraZeneca

AstraZeneca United States purchased one ICR12000 & six ICR8000 from Aurora for high-throughput screening (HTS) of compounds. After comparison between all the HTS assay sv ailable today to study NaV channels, results suggest that the Li-AAS assay is more suited as a primary HTS assay when study ing NaV drug discov ery campaign.

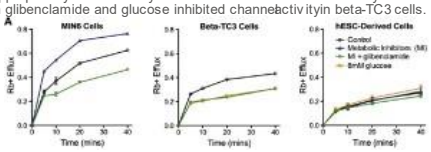


Testing 80 ion channel modulators for activity against KCNQ2. The solid line represents the average % efflux of all samples. The dashed line represents 20% inhibition of stimulated efflux. It was found that there were four compounds below this critical value, which provided a basis for further concentration-dependent experiments.

Measurement of Potassium Channel Activity in hESC-derived Stem Cell Model

THE UNIVERSITY OF BRITISH COLUMBIA

K_{ATP} channel activity was determined by measuring Rb+ efflux over time. hESC-derived cells were not responsive to either K_{ATP} channel inhibitors (glibenclamide and glucose) or activators (metabolic inhibitors: oligomycin and 2-deoxy-D-glucose). In contrast, K_{ATP} channel activity in MIN6 β-cells was appropriately stimulated by metabolic inhibitors and inhibited by the addition of glibenclamide; both glibenclamide and glucose inhibited channel activity in beta-TC3 cells.



User Cases

MERCK

Merck Pharmaceutical Company of Germany has a ICR8000, to work with patch clamp technology in drug screening and drug mechanism research. ICR8000 is used for high-throughput ion flux analysis and the patch clamp is used for more in-depth electrophysiological analysis. The research results found in many published academic papers include- The discovery of different groups of benzopyranrings on the role of hERG K+ ion channels, the study of voltage gated potassium channel Kv 1.5 and drug DPO-1, PAC, correolide binding regions and related mechanisms.
Original research: High throughput analysis of drug binding interactions for the human cardiac channels, Kv 1.5

Wyeth

Wyeth a famous pharmaceutical and biological company that uses ICR8000 to screen KCNQ/MK+ ion channel blockers. Compared with the effect of the patch clamp, the positive correct coefficient of the ICR is r=0.60, which proves that the method is reliable. Moreover, the treatment flux of ICR is larger than that of the patch clamp, which is very suitable for secondary screening and analysis of drugs.
Original research: Validation of an Atomic Absorption Rubidium Ion Efflux Assay for KCNQ/MChannels Using the Ion Channel Reader 8000

Roche

Roche Switzerland launched high throughput screening of more than one million drugs in 2013. After learning about Aurora's Ion Channel Reader technology senior laboratory technicians were sent to Aurora Canada Headquarters for experimental verification. The experimental data rapidly obtained was significant. Therefore, Aurora's high throughput ion channel reader ICR12000 was ordered and installed at their Swiss headquarters to speed up the drug screening process.

ICR8000 was purchased by the well-known ion channel research team in China, Pharmacology Research Department of Hebei Medical University. ICR8000 was initially used for high throughput screening of calcium-activated chloride channel TMEM16A and its regulatory factors. In comparison with other ion channel research technologies ICR has the advantages of high throughput good repeatability, safety, accuracy and simple operation.
Original research: Development and validation of HTS assay for screening the calcium-activated chloride channel modulators TMEM16A stably expressed in CHO cells

Tu Youyou, a Chinese scientist won the Nobel Prize in Physiology or Medicine in 2015 for her "Discovery of Novel Therapy Against Malaria". Aurora's ICR8000 was purchased by the institute of the Chinese Academy of Medical Sciences for the research and development of natural compound medicine against malaria and immunity diseases.