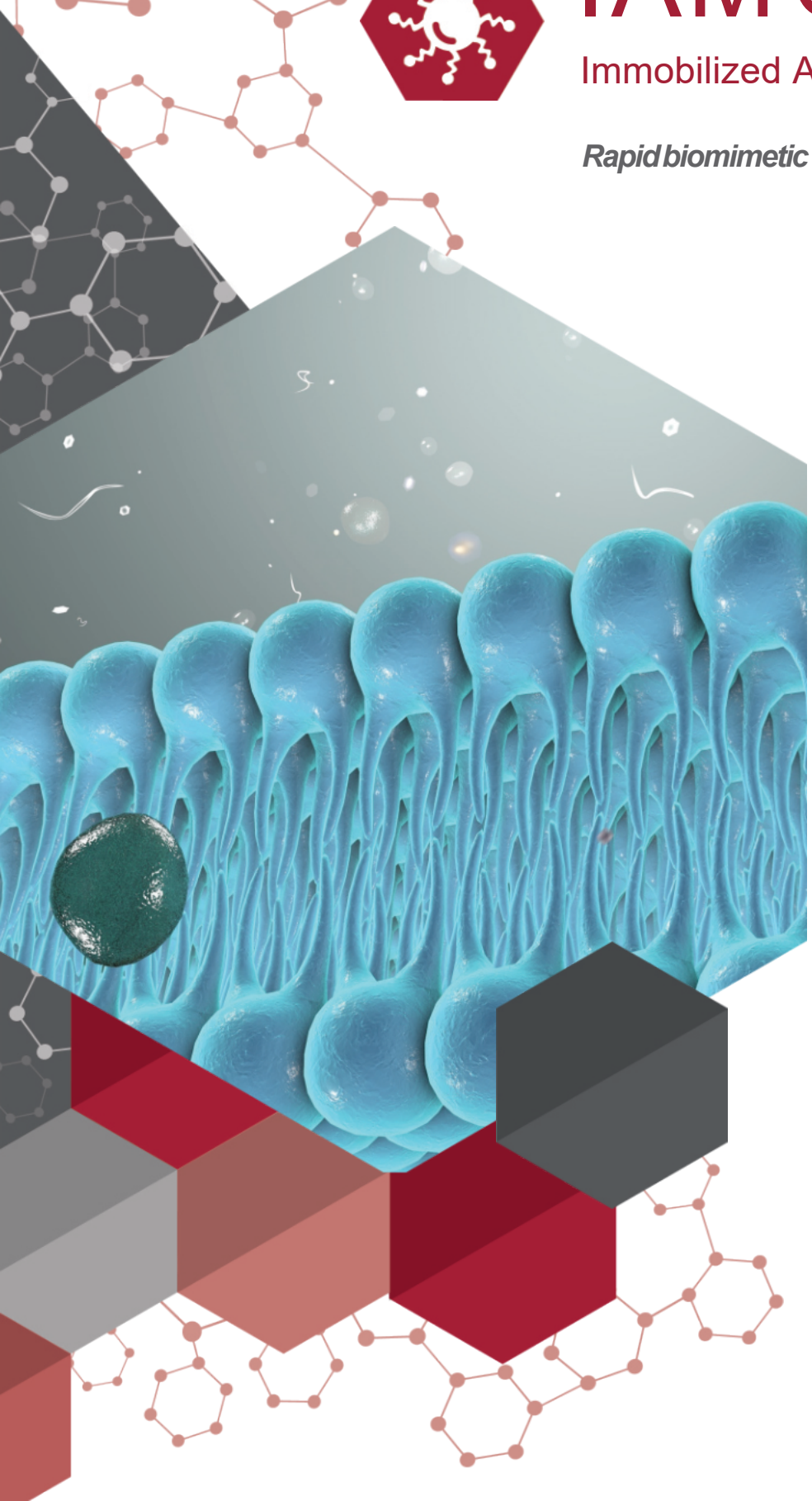
IAM Columns

Immobilized Artificial Membrane Columns

Rapid biomimetic screening of drug-membrane affinity



AN ADVANCED TOOL FOR DRUG DISCOVERY

Accelerate Drug Discovery

Speed Compound Selection

Reduce Attrition at Late Stage

Limit the Number of Animal Studies

REGIS® TECHNOLOGIES, INC.

IAM

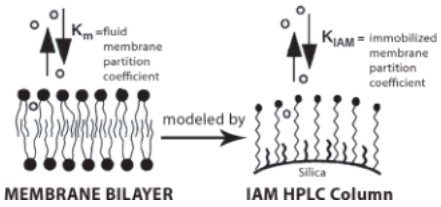
BENEFITS FOR DRUG DISCOVERY

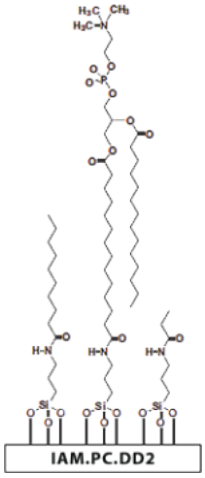
- Rapidly screen drug/phospholipid interactions
- Identify suitable compounds early in the process
- Identify and eliminate compounds with low permeability
- Predict *in vivo* compound behavior, reducing need for animal studies

As phospholipids are major components of tissues and cells, drug interaction with phospholipids is an important contributor to distribution. Immobilized Artificial Membrane (IAM) chromatography can be used to quickly measure drug-phospholipid interactions via retention times.

IAM COLUMN STATIONARY PHASE CHARACTERISTICS AND USES

- Emulates the lipid environment on a solid surface
- Covalently bonded Phosphatidylcholine (PC) to silica
- Highly stable stationary phase suitable for thousands of injections

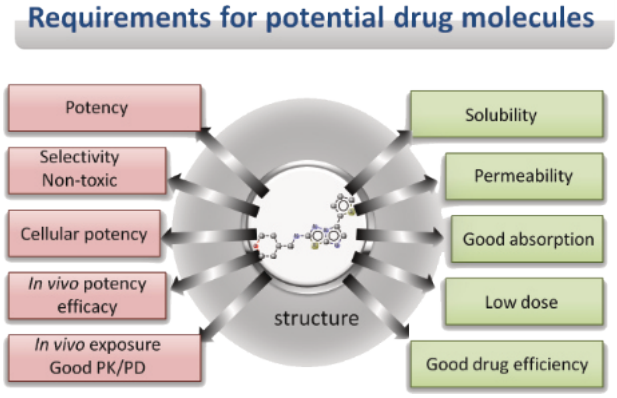




- Retention on the IAM stationary phase can be directly related to membrane partition coefficients
- Thousands of drug discovery compounds can be characterized by IAM retention time measurements
- Normalized retention times are used for ranking compounds

DRUG/PHOSPHOLIPID BINDING CAN INFLUENCE:

- Permeability
- Absorption
- Solubility enhancement
- Toxicity
- Volume of distribution
- Drug efficiency
- Cellular potency



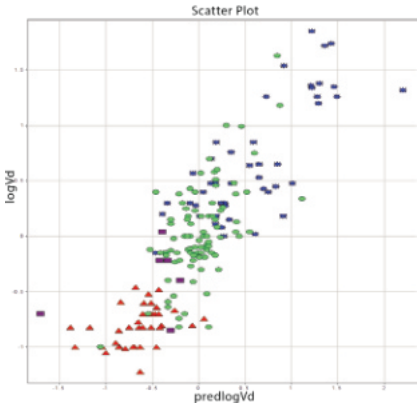
Quickly set up IAM screeningto get an early indication of drug membrane interaction:

- Inject a calibration mixture and run a simple gradient
- Plot the calibration curve
- Inject your drug compound under the same conditions and obtain K values
- Using supplied equations the drug sample is then compared to known binding models

Detailed proceduresare provided in our userguide.

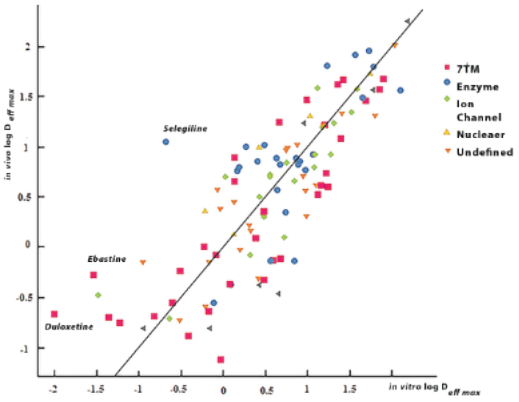
IAM chromatography is a simple and reliable tool to measurephospholipid/ drug affinity via calibrated retention times on IAM stationary phases. Regis Technologies IAM Columns are high quality, long lasting HPLC columns providing reliable measurements across a wide range of drug molecules. A calibration mixture and instructions how to obtain and use the critical information of drug discovery compounds are also available.

VOLUME OF DISTRIBUTION MODEL



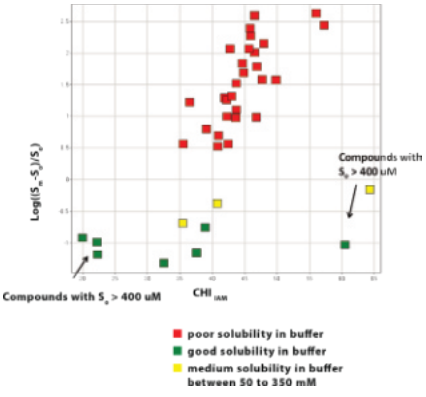
Human clinical steady state volume of distribution (logVdss) data of 130 marketed drug molecules showstrends with the estimated values using IAM and HSA binding data.

DRUG EFFICIENCY MODEL



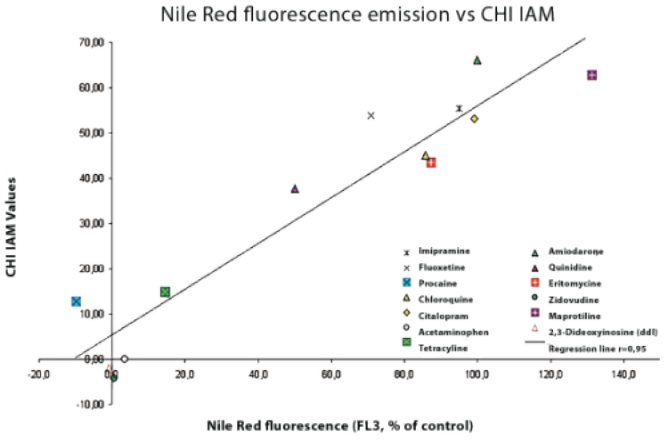
The sum of the IAM and HSAbinding of compounds models the *in vivo* drug efficiency.

SOLUBILITY ENHANCEMENT BY MICELLES IN SIMULATED INTESTINAL FLUIDS



The intestines contain phosphatidyl choline micelles that enhancethe solubility and absorption of nutrients. Solubility enhancement shows good correlation to IAMbinding of compounds.

PHOSPHOLIPIDOSIS TOXICITY POTENTIAL



CHI IAM values higher than 50 indicate phospholipidosis potential. Phospholipidosis is an accumulation of lamellar phospholipidsin the cell often causedby drugs.Hepatotoxicity caused by phospholipid accumulation detected by Nile Red fluorescence shows excellent correlation to CHIIAM values.

IAM

Rapid biomimetic screeningof drug-membrane affinity
An advanced tool for drug discovery

PRODUCT	Dimensions	Particle Size	IAM.PC.DD2 Catal o g #	IAM.PC Catal o g #	IAM.PC.MG Catal o g #
Columns	15 cm x 3 mm	10 µm	1-774004-300	N/A	N/A
	10 cm x 3 mm	10 µm	1-774003-300	N/A	N/A
	3 cm x 4.6 mm	10 µm	1-774010-300	1-770007-300	1-772007-300
	10 cm x 4.6 mm	10 µm	1-774011-300	N/A	N/A
	15 cm x 4.6 mm	10 µm	1-774014-300	1-770001-300	1-772001-300
Guard Kit	1 cm x 3 mm	10 µm	1-774012-300	1-771001-300	1-773001-300
Guard Cartridges	1 cm x 3 mm	10 µm	1-774013-300	N/A	N/A
IAM FastScreen Mini Column Kit*	1 cm x 3 mm	10 µm	1-775014-300*	N/A	N/A
Drug Screening Calibration Mixture	10 x 1 mL	N/A	1-774015-300	N/A	N/A

* Not associated with one type of IAM phase. Inquire for more details.

Useful References for Drug Membrane Affinity Screening with IAM

1. Valko et al. Rapid-gradient HPLC method for measuring drug interactions with immobilized artificial membrane: comparison with other lipophilicity measures. *Journal of Chromatographic Sciences* **2000,** *89,* 1085-1096.
1. Tsopelas et al., Advances in immobilized artificial membrane (IAM) chromatography for novel drug discovery, *Expert Opinion in Drug Discovery* **2016,** DOI: 10.1517/17460441.2016.1160886
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1. Hollosy et al. Estimation of Volume of Distribution in Humans from High Throughput HPLC-Based Measurements of Human Serum Albumin Binding and Immobilized Artificial Membrane Partitioning. *Journal of Medicinal Chemistry* **2006,** *40,* 6968-6071.
1. Valko et al., Fast Gradient HPLC Method to Determine Compounds Binding to Human Serum Albumin. Relationships with Octanol/Water and Immobilized Artificial Membrane Lipophilicity, *Journal of Pharmaceutical Sciences,* **2003**, *92*, 2236-2248.
1. Valko et al. *In vitro* measurements of Drug Efficiency Index to Aid Early Lead Optimization. *Journal of Pharmaceutical Sciences* **2012,** *101,* 4155-4169.
1. Casartelli et al. A cell-based approach for the early assessment of the phospholipidogenic potential in pharmaceutical research and drug development, *Cell Biology and Toxicology* **2003,** *19*, 161-176.
1. Valko, K., *Physicochemical and Biomimetic Properties in Drug Discovery; Chromatographic Techniques in Lead Optimization*; Wiley: Hoboken, NJ, 2014; pp 134-140.

Add Regis'IAM columns to your drug discovery tool box today!

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