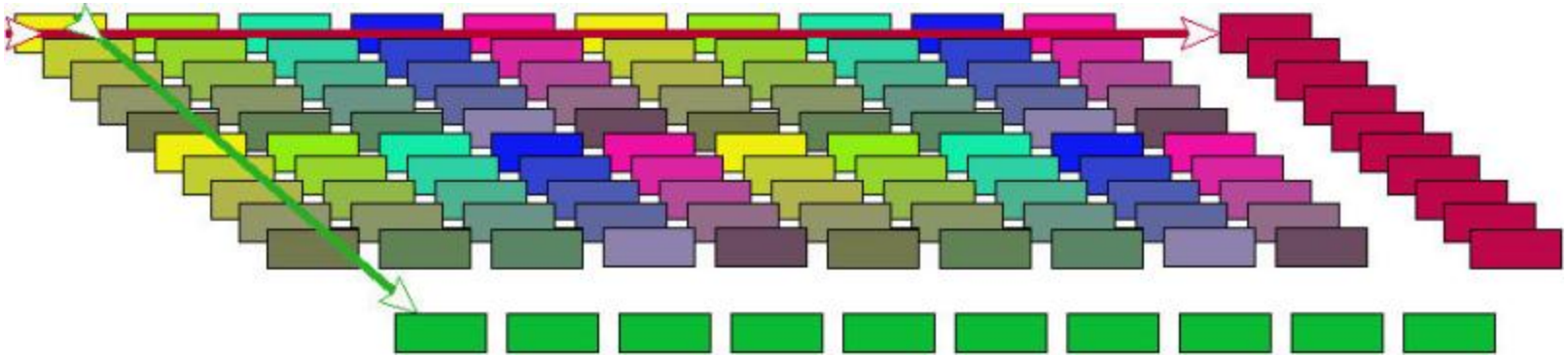
Orthogonal Pooled Screening

HTS with 5X higher efficiency, 5x lower costs

Orthogonal Pooled Screening (OPS): 5x higher efficiency, 5x lower costs

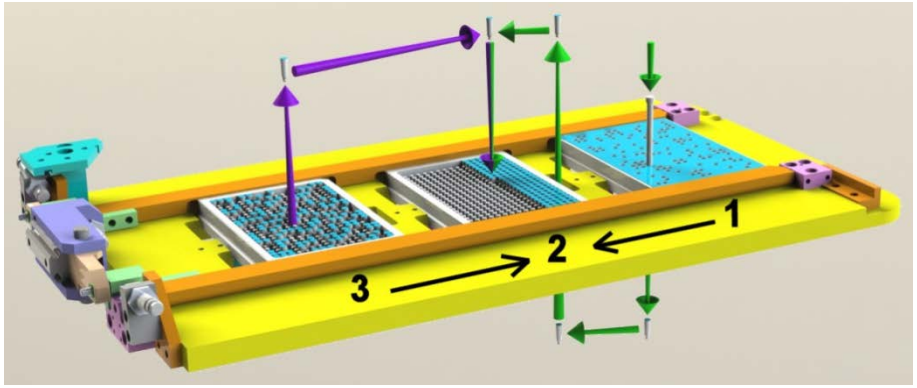
- We offer this technology as a turnkey HTS-support service, including access to our rare compound collections and gamut hit-to-lead follow-on support.
- This offers a markedly more efficient and cost effective way to find new drug leads with remarkable speed.
- We are blind and have no interest to any IP arising from OPS; our fair consideration is simply a fee for services delivered successfully.
- Contact us directly to understand how we can apply OPS in non-obvious ways to benchmark, and then measurably enhance quality of data throughout your organization.

What is Orthogonal Pooled Screening (OPS)?



- Each well contains 10 compounds from a 150,000 compound diversity library.
- Each compound is present in two wells, amongst a unique combination of 9 other compounds.
- To be tallied as a hit, the compound must show reactivity in both wells.
- The net result is a five-fold reduction in screening volume (e.g., 8,000 compounds in six 384 well plates), with n=2 corroboration.

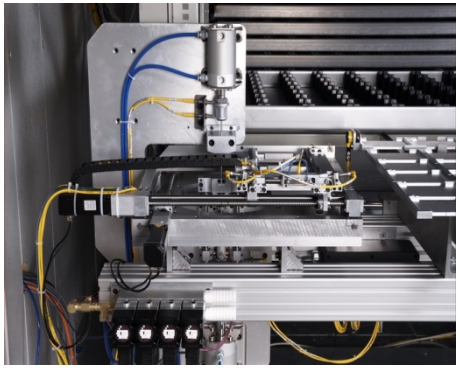
Why use the Service?



- Reduces screening volume 5x, saving you time, reagents and money—minimum of 80% cost savings guaranteed. Expert guidance is provided by LCGC to GUARANTEE success.
- Allows more compounds to be screened, increasing chemical diversity and probability of quality hits.
- Eliminates the need for HTS infrastructure; e.g., robotics and compound management.
- Leverages state-of-the-art data mining software and chemoinformatic expertise to accelerate lead finding.

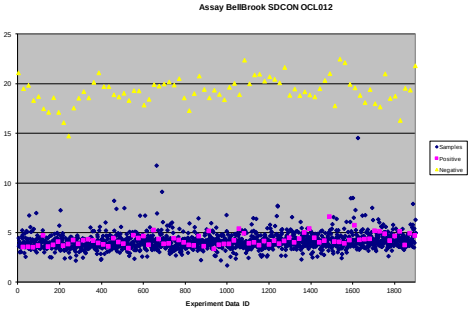
How does the Service work?

Client /Collaborator defines project: number and type of compounds, type of plates

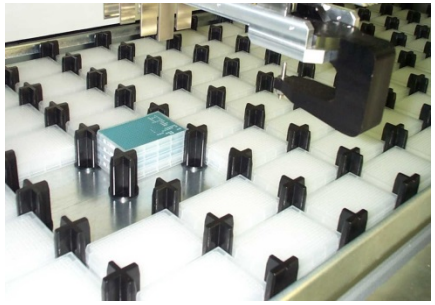


Assay-ready OPS plates are prepared by LCGC and shipped to Client

Client runs assays and sends raw data and hit cutoff parameters



Data are de-convoluted by LCGC and SAR table is sent to Client for review.



Hits are cherry-picked at LCGC and individuals are sent to Client for confirmation of activity.

- ***Uses only 1/5th the resources***
- ***Expert consulting included***
- ***Data held confidential***
- ***LIMR is blind to targets***
- ***LIMR receives no IP rights***
- ***Client solely owns new IP***
- ***Discounts for multiple screens***

➢ ***Try before you buy: success is guaranteed***

Why use the LCGC library?

- High analytical quality: >85% are pure compounds
- Drug like properties: Vast majority of compounds pass all Lipinski rules and drug reactivity filters, average MW is < 300.
- Diversity and novelty: More than 60% are novel scaffolds not found in commercial collections
- Extensively validated: Average hit confirmation is 72% for biochemical assays, and up to 95% for cellular assays
- Rigorous confirmation: Hits are cherry picked for confirmation without freeze/thawing; powder reserves support second tier confirmation.
- Secure IP: LCGC operates blinded to structure with no IP reach through. ***'Try-before-you-buy' assures transparency and lead-discovery success, with no risk.***

Try an OPS Pilot Run in Your Assay at No Cost and No Risk

- We supply a tester set of OPS compounds containing 8,000 compounds in duplicate on five 384-well microtiter plates.
- Pre-arrayed ‘dots’ (0.3-1.0 μL) are provided to scientists in your lab—or to a CRO you designate. Reagents are added by your staff, who run the assay and then send us the data for de-convolution on Excel templates we provide to you.
- We then deliver the hit list and SAR table for your review, and will also provide the cherry picked, individual samples for retesting at no additional cost. If client is satisfied, we can then proceed to a full HTS campaign.
- This model can be quickly executed: Two weeks from purchase order approval to completion—including concentration-response testing.

What kind of results can I expect from OPS?

Assay	Cutoff	Actives	Best Potency	Confirm Rate
E7 DNA Binding (ELISA)	20%	63	< 1 μM	77%
Sugar Kinase (FP)	50-70%	48	1 μM	66%
Cathepsin C (FP)	50%	64	5 nM	88%
ATP Synthase (Lucif)	80%	16	< 500 nM	100%
USP-7 (FI)	85%	140	500 nM	56%
CXCR2 (cellular)	50%	7	5 nM	100%
ARE-LUC (cellular)	40%	16	440 nM	96%
mTb (cellular)	90%	9	< 1 μM	88%

OPS Published Studies

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5. Thompson S, Messick T, Schultz DC, Reichman M, Lieberman PM. Development of a high-throughput screen for inhibitors of Epstein-Barr virus EBNA1. J Biomol. Screen. 2010;15:1107-15. PMID: 20930215
6. Fera D, Schultz DC, Hodawadekar S, Reichman M, Donover PS, Melvin J, Troutman S, Kissil JL, Huryn DM, Marmorstein R. Identification and characterization of small molecule antagonists of pRb inactivation by viral oncoproteins. Chem. Biol. 2012. 19:518-28. PMID: 22520758
7. Donover PS, Yohn M, Sim M, Wright A, Gowda S, Allee C, Schabdach AR, Reichman M. New informatics and automated infrastructure to accelerate new leads discovery by high throughput screening (HTS). Comb Chem High Throughput Screen. 2013;16:180-8. PMID: 22934945.
8. Reichman M, Schabdach A, Kumar M, Zielinski T, Donover PS, Laury-Kleintop LD, Lowery RG. A High-Throughput Assay for Rho Guanine Nucleotide Exchange Factors Based on the Transcreener GDP Assay. J Biomol Screen. 2015 Dec;20(10):1294-9. doi: 10.1177/1087057115596326. Epub 2015 Jul 20. PubMed PMID: 26195453.
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10. Cheng N, Lee SK, Donover PS, Reichman M, Schiffer CA, Hull-Ryde EA, Swanstrom R, Janzen WP. Development of a Novel Screening Strategy Designed to Discover a New Class of HIV Drugs. J Lab Autom. 2014 Jun;19(3):297-303. doi: 10.1177/2211068213513453. Epub 2013 Dec 4. PubMed PMID: 24305957; PubMed Central PMCID: PMC4216240.
11. Zielinski T, Reichman M, Donover PS, Lowery RG. Development and Validation of a Universal High-Throughput UDP-Glycosyltransferase Assay with a Time-Resolved FRET Signal. Assay Drug Dev Technol. 2016 May;14(4):240-51. doi: 10.1089/adt.2016.711. Epub 2016 May 2. PubMed PMID: 27136323.

Other OPS Services

We offer a proprietary method to detect unexpected drug synergies between drugs and specially-selected, purified natural products.

In addition:

Synergy studies: Automated drug combination studies (*Chau Telalay)*

✓Combination Index
✓Isobolographic Analysis
✓ Dose Reduction Index
✓Conditioned screening with RNAi or any compound of choice
✓ Drug-Drug (generic, branded, OTC) and Drug-Nutraceutical Synergy

Contact for more detail:
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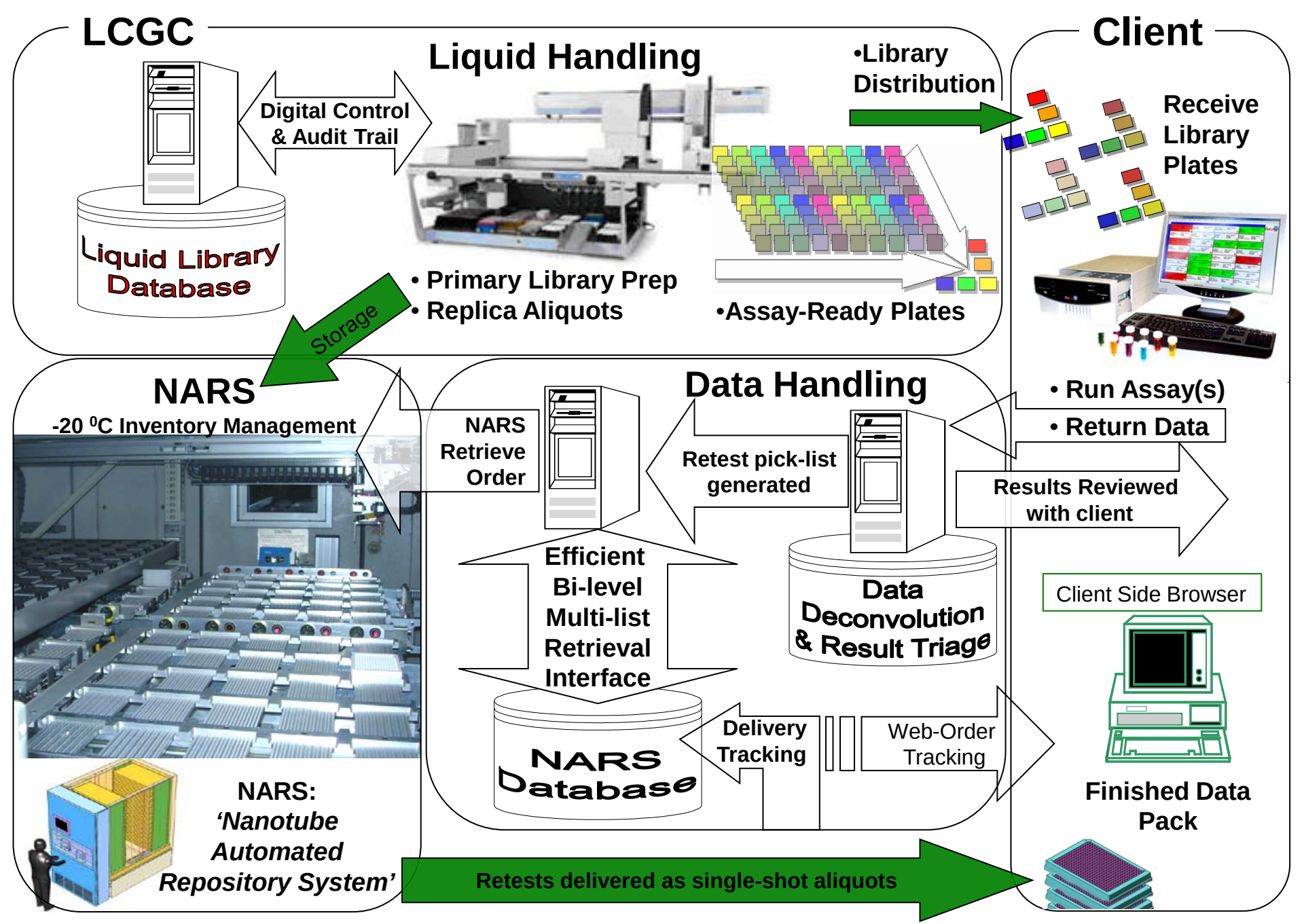

Automated Infrastructure Accelerates New Leads Discovery by High Throughput Screening.