Cancer Drug Discovery

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Drug Discovery at the Brown Cancer Center
How we use the Dataseam Grid.

Drug Discovery: Virtual screening.
Use computers to find potential drugs that block cancer target structures.

Why?
It is faster and cheaper than traditional discovery.

**Faster:** Speed is linear to number of computers.
Dataseam Grid: 10,000 dedicated virtual screening processor cores

**Cheaper:** We buy in 100 compounds, not millions.
Routine Libraries to screen
ZINC Drug-Like: 24,877,119 compounds
Pubchem: 97,000,000 compounds

Does it work….and do Researchers use it?

The pipeline of targets that have been virtually screened and inhibitors have been found experimentally at the BCC by these research groups listed by PI. (Multiple listing means multiple targets.)

- Chesney
- Telang
- Trent
- Bates, Miller, Trent
- Chesney
- Mitchell
- Clem
- Bodduluri
- Clark
- Clark
- Donninger
- Chaires
- Chaires, Trent
- Bates
- Lane, Fan
- Mitchell

- Clem
- Li, C.
- Tooley
- Jonsson
- Grimes
- Hein
- Hein
- States
- Eaton
- Beverly
- Lillard
- Learner
- Zundel
- Clark
- Ceresa
- Li, B.
- Trent, Chaires

Dataseam Grid Benefits to Research.

- Increases research capacity up to 10-fold.
- Makes research nationally competitive for Federal grants using a unique resource.
- Generates data making Federal Grant Applications possible.
- Attract and retain expert researchers.
- We can perform new research that we would not pursue without it.

Two targets 1) Phase I Clinical Trial 2014, 2) Phase I Clinical Trial 2018
Ras Pathway: Another Holy Grail.

G. Clark and J. Trent

Ras is one of the most important cancer genes
Mutant Ras in Cancer: Lung 30%, Liver 30%, Pancreas 90%, colon 50%.

List of indirect RAS inhibitors tested in clinical trials.
All prove disappointing so far.

Targeting the Ras – Ral Pathway
Selected 500 compounds, tested 48, 2 inhibitors Ras:Ral protein-protein complex.
Ras Pathway: Another Holy Grail.

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History.

2007 - 2010: Drug Discovery: Brown Cancer Center NIH Molecular Targets COBRE (2003-2018 $26M)


2018-2020 NIH R21 grant ($423K)

2019-2023 KYNETIC Program: Kentucky Network for Innovation and Commercialization 2019-2023 $6.56M ($3.96M NIH, $1.8M KY state, $400K UK and UL)


Pending

Brown Cancer Center NIH CCII: Center for Cancer Immunology & Immunotherapy COBRE Award ($11.5M 2020-2025)
Progress (since Jan 1, 2010)

- 382 screens, 6,256,770,745 compounds screened against Protein and DNA targets
- Found inhibitors to over 50 protein and DNA targets.
- Licensed/optioned six compound family’s IP to Biotech
- Second drug entered cancer clinical trials (May 2014); PFK-158 targeting PFKFB3 (Trent/Chesney/ACT)
- Third drug/product Biotech Product in clinical development (2018-).

Dataseam Partnership with Brown Cancer Center:
- WIN for Cancer Research
- WIN for K-12 Students:
- WIN for Kentucky:
Datastream Participating Counties

- Participation as of July 1, 2019
- Expansion July 1, 2019 > Present
“Thank You!”

Dataseam Partner Districts, University of Louisville, University of Louisville Brown Cancer Center, Morehead State University, Morehead Space Sciences, Dataseam Scholars and Educators.