

# *“The Ultimate Deliverable: Translation of Personalized Medicine Technology to the Clinic & Patient”*

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# What is personalized medicine made of? What can it deliver? Who is delivering?



*"The Case for Personalized Medicine"*  
– Personalized Medicine Coalition



- Personalized medicine, the basics..
- The promises of personalized medicine.
- Which “promises” are translating to reality – some exciting selected examples.
- Perspectives on the near term future..

# The Basic Foundation

*How is personalized medicine technology translated to the bedside?*

## Goals



**Enhanced ability to detect disease**



**Optimized therapies that increase efficacy**

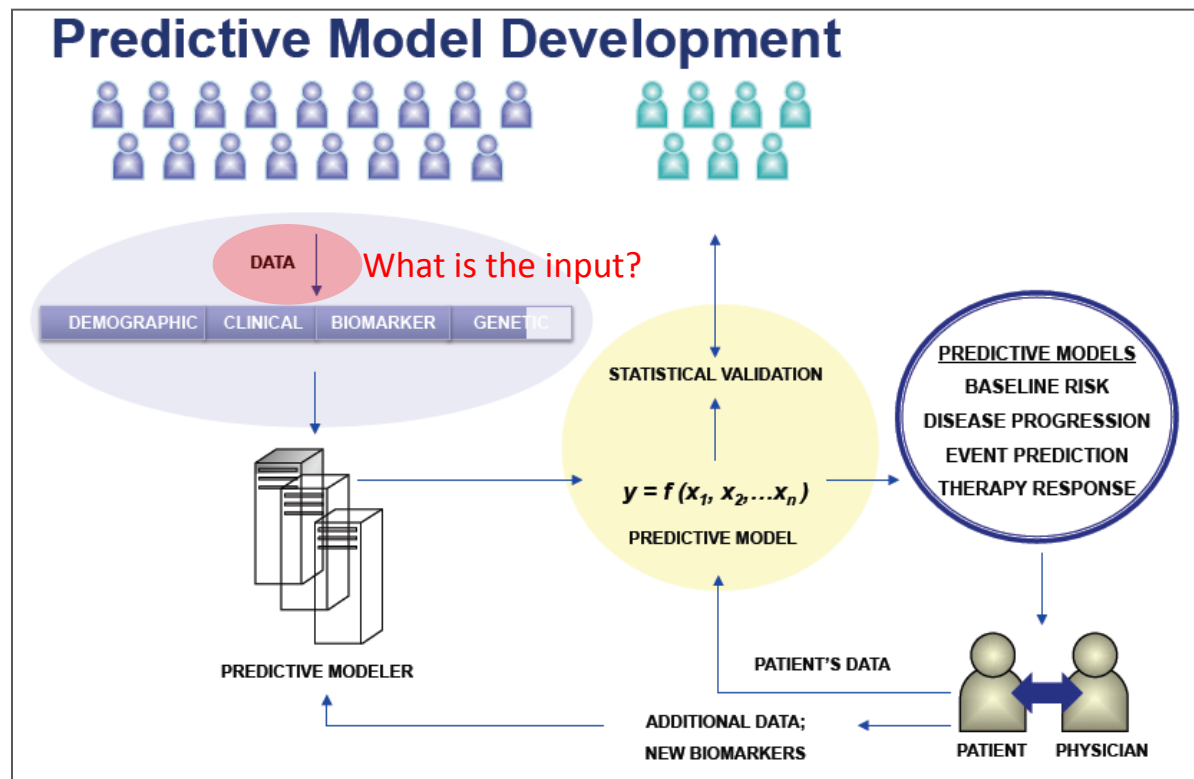


**Deeper understanding of disease subtypes & risk predisposition**



**Longitudinal management of an individual's health**

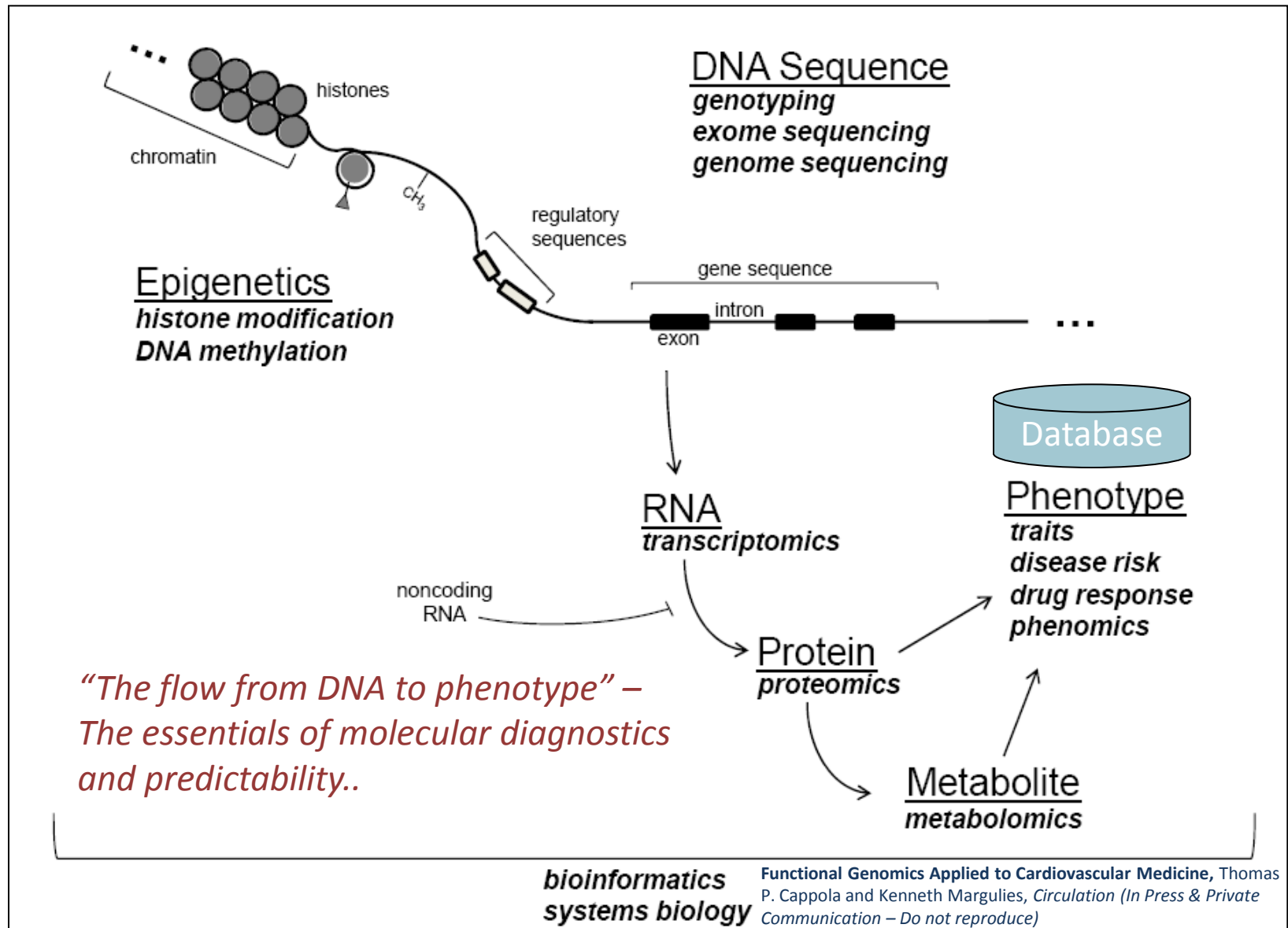
## Paradigm Development



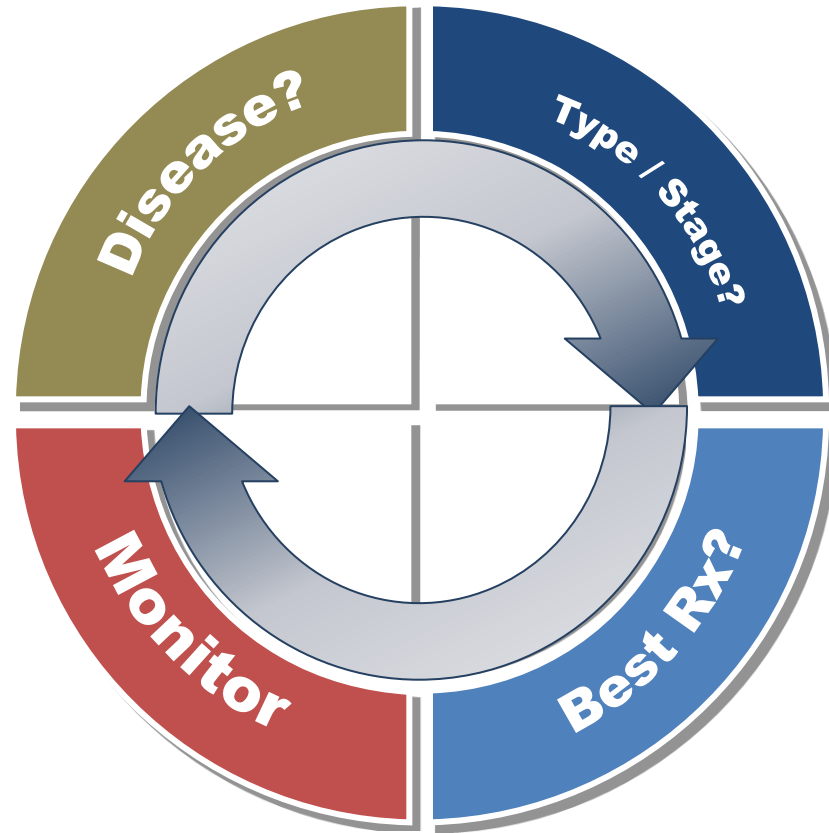
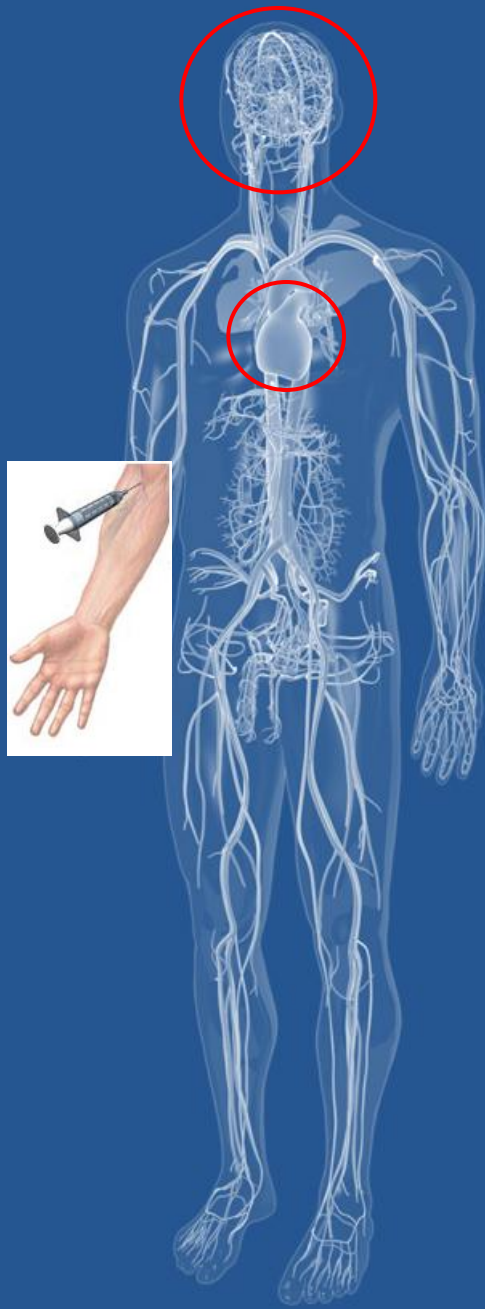
Executive Performance Webinar Series:  
Clinical Leadership Education Sessions

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# The Molecular Components of Personalized Medicine



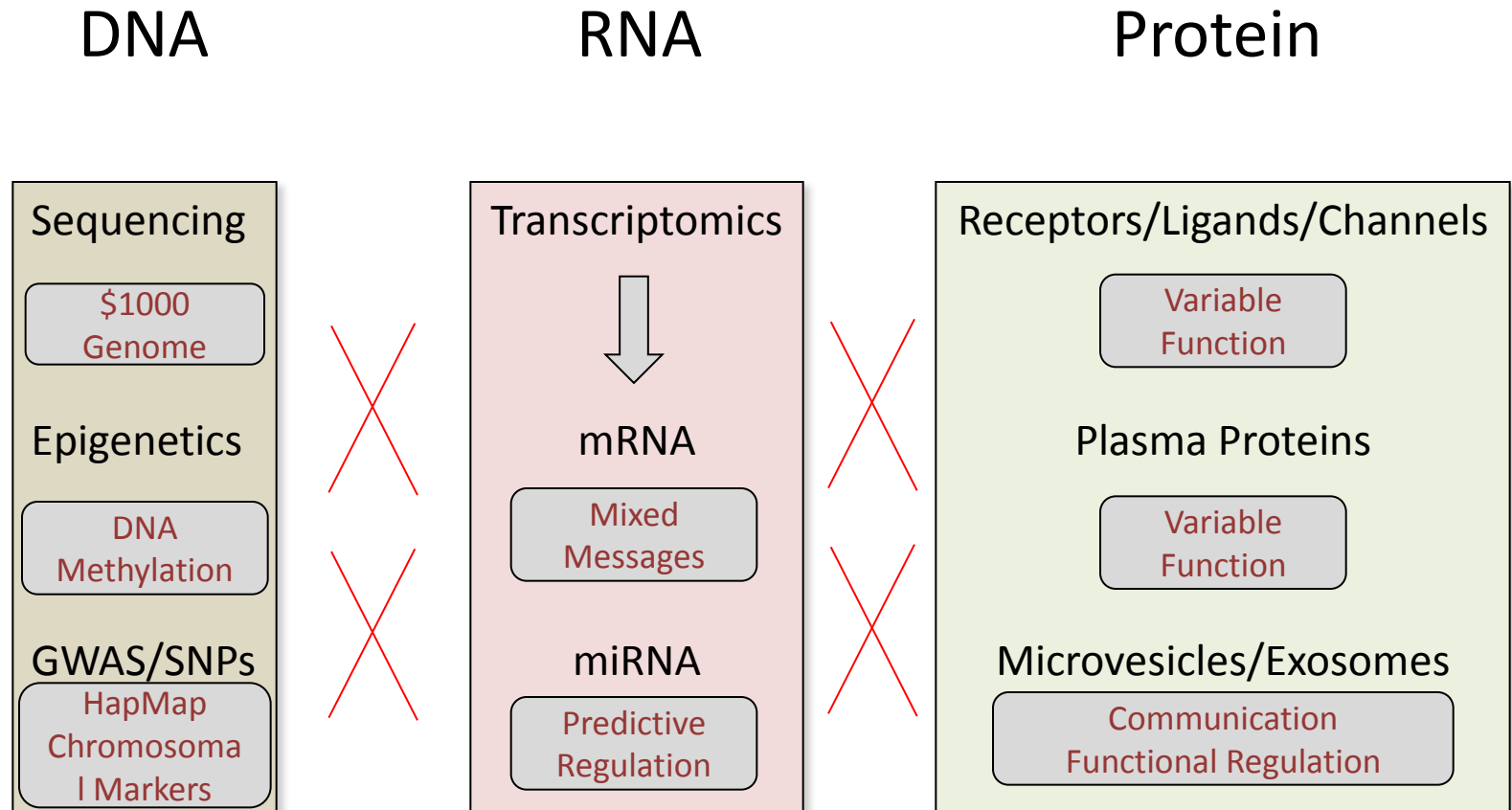
# Systems Biology: Creating predictive sense and translatable commercial value



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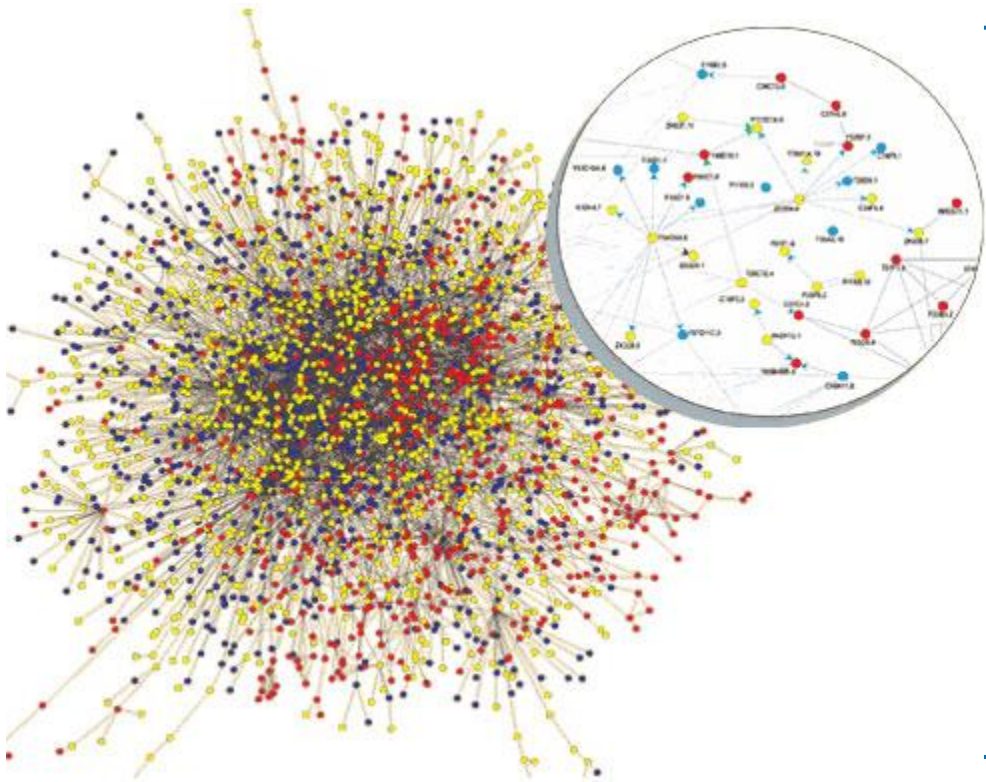
# How to Inform Personalized Medicine?



All part of the “*flow to individual phenotypes*” – Each interacting in a complex network governed by each other → “*Interactome*”



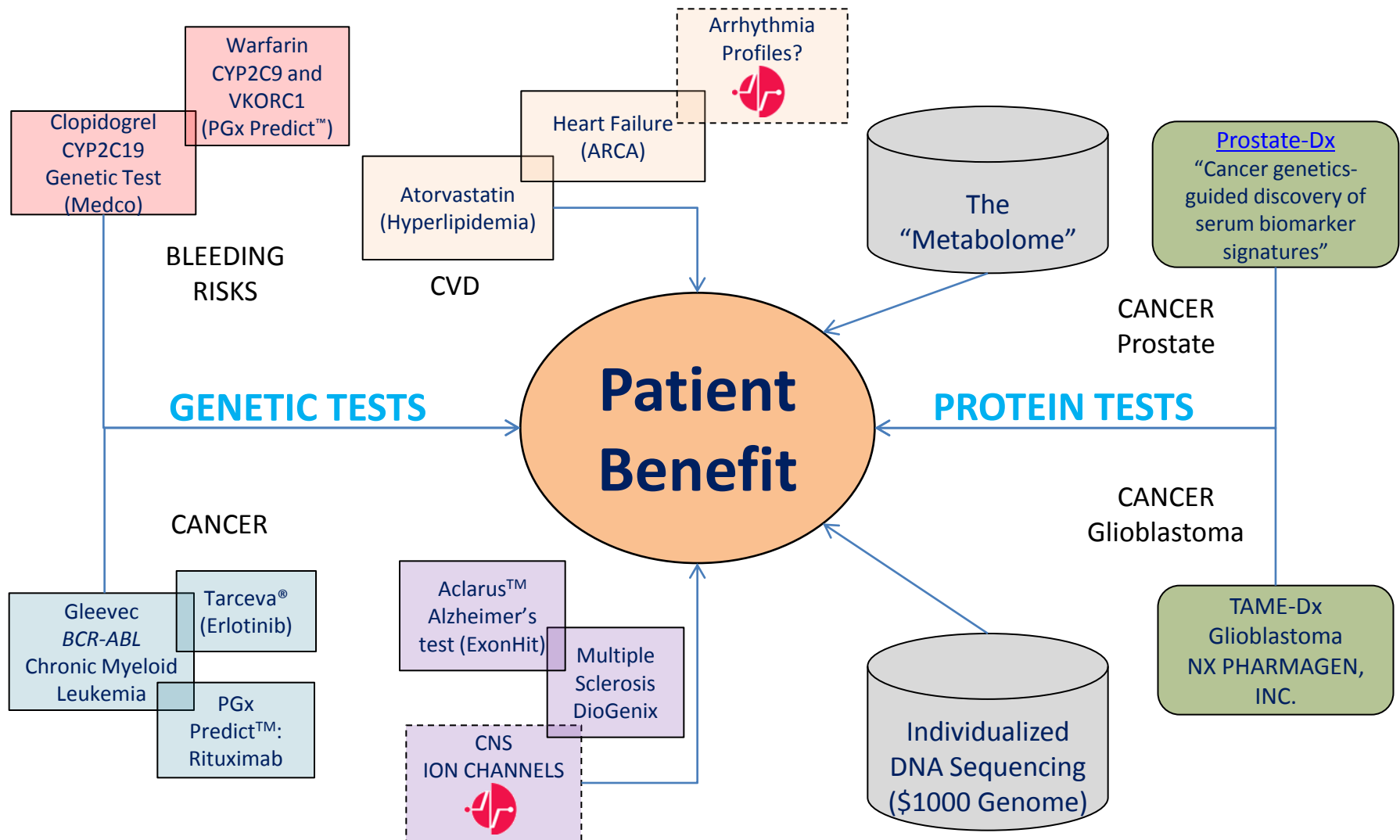
# Interactome? How can this be translated to the bedside?



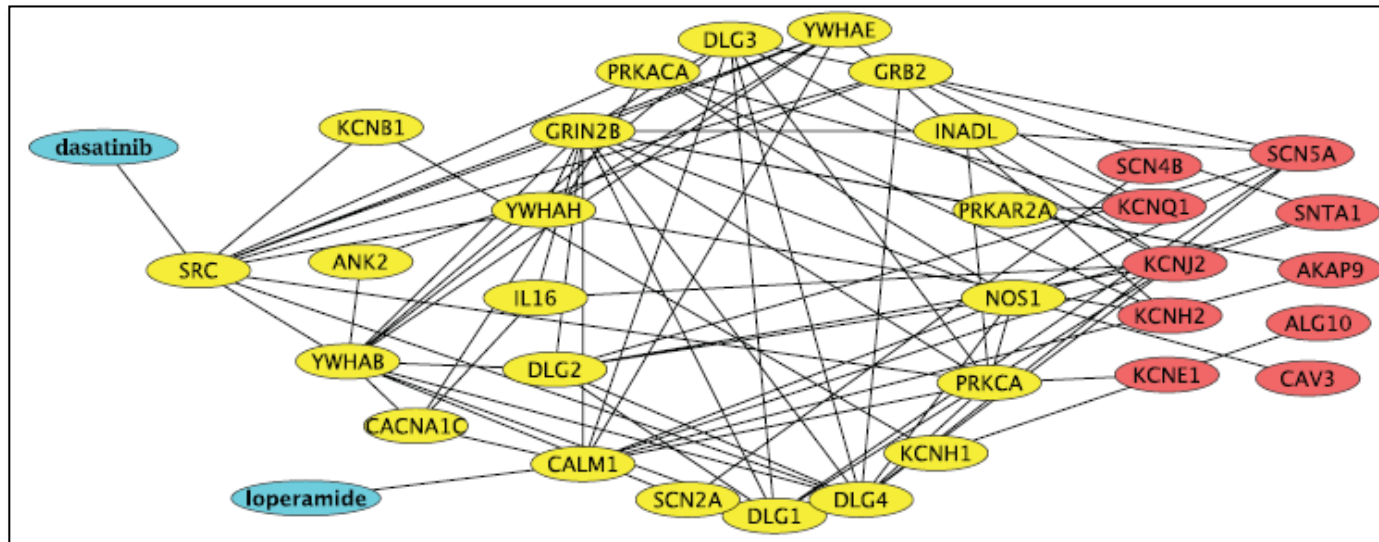
*“The cell doesn’t function purely by the action of individual proteins, but instead by large macromolecular complexes mediated by many interacting proteins” - Pawel Smialowski, The Negatome database: a reference set of non-interacting protein pairs. Nucl. Acids Res. (2009).*



# Current Tests: “Cherry-Picking a Few..”



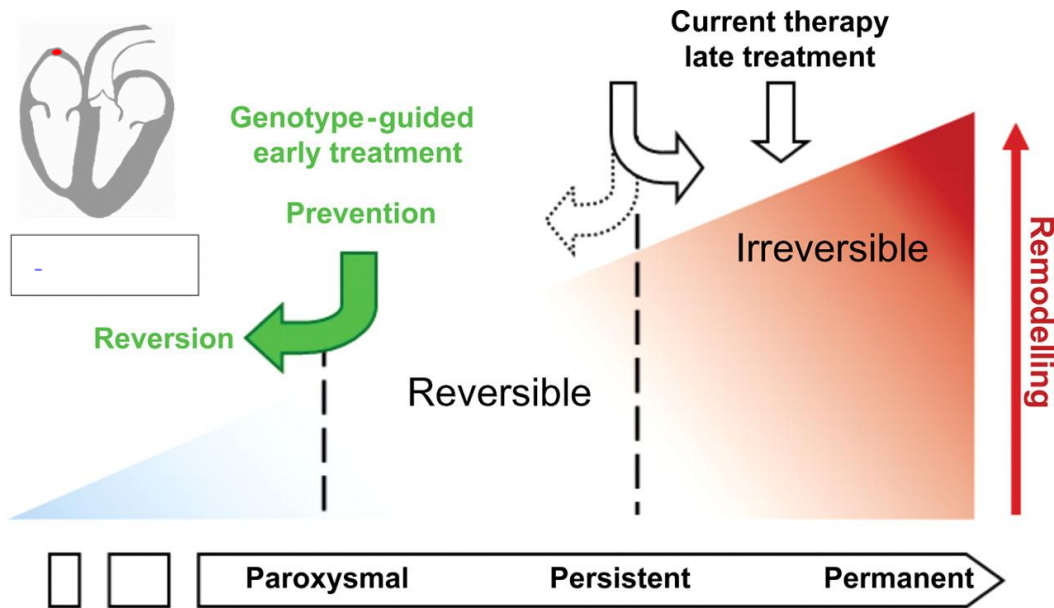
# Heart Disease



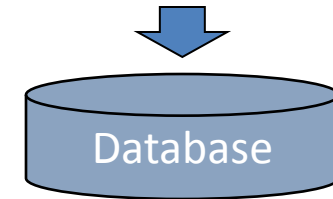
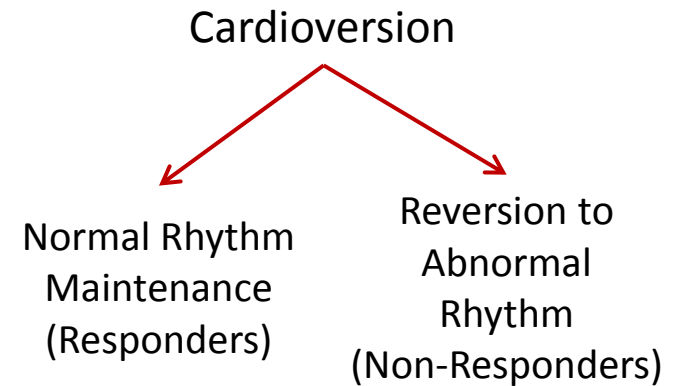
An interactome of genes that play a role in LQTS drug-induced changes in electrical activity of the heart leading to fatal arrhythmias - The use of the “*LQTS neighborhood*” to classify and explain FDA adverse event reports.

From: “*Systems Pharmacology of Arrhythmias*”, Seth I. Berger, Avi Ma’ayan and Ravi Iyengar (20 April 2010) Science Signaling 3 (118) Department of Pharmacology and Systems Therapeutics and Systems Biology Center New York, Mount Sinai School of Medicine, One Gustave L. Levy Place, Box 1215, New York, NY 10029, USA.

# Cardiome Pharma Corp.- Arrhythmia Biorepository



Sinner, M.F., et al. (2011), *Cardiovasc Res* 89 (4): 701-709.



## Vernakalant Genetic Sub-Study (Human blood):

~680 Patients → RNA/DNA Isolation → SNP Analysis/Expression Profiling

- Identifying responder/non-responder populations
- Stratify clinical trials
- Predictive prognostication
- Individualized DNA sequencing

## Cardiac Remodeling (Animal Models):

Drug-mediated inhibition or reversal of maladaptive cardiac remodeling

- Defining “the line” between reversible and irreversible AF
- Tailoring treatment as a function of remodeling

Regulation of key channels and cofactors/subunits, maladaptive remodeling factors.

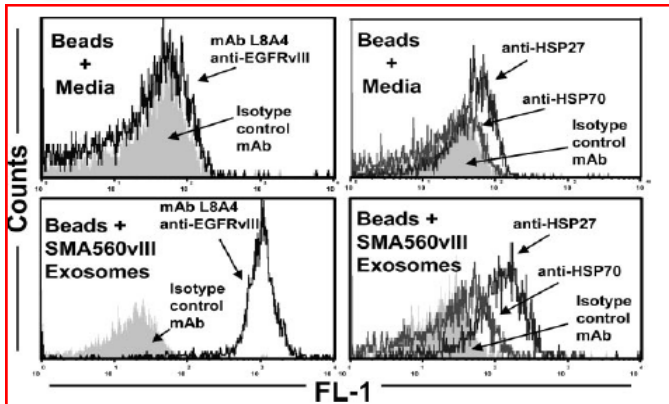
# It's not just proteins anymore..



**TAME-DX**



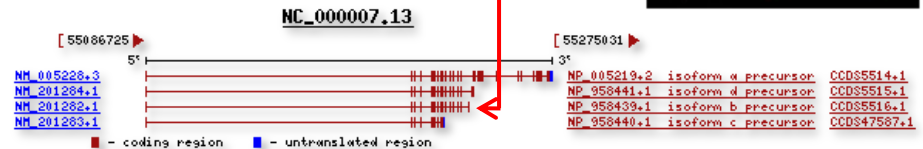
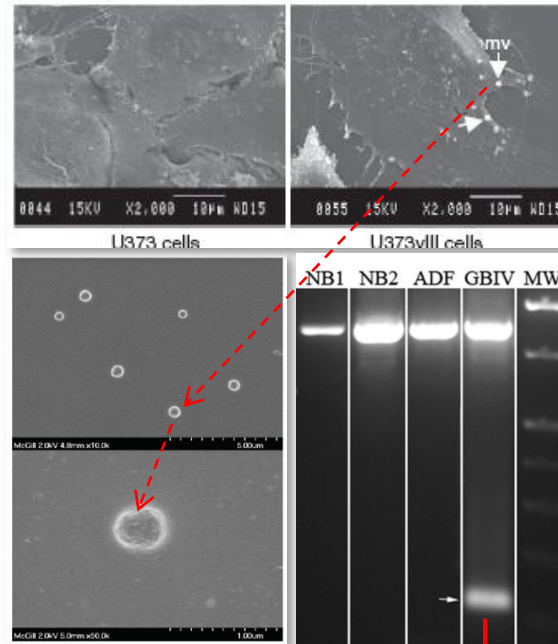
Alan Ezrin, PhD  
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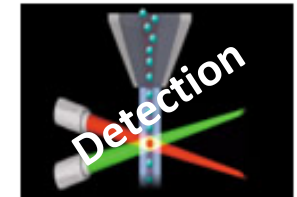
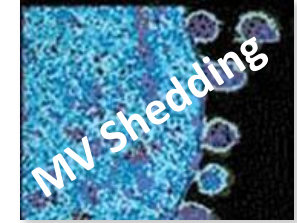
[Michael W. Graner, et al. May 2009 The FASEB Journal vol. 23 no. 5 1541-1557.](#)

## BRAIN CANCER (Glioblastoma multiforme)

- > 99% Fatal, ~2% surviving longer than three years after diagnosis.
- Early detection/Recurrence monitoring
- Prognostic / classification / longitudinal data
- Treatment response/non-response



[Janusz Rak, et al. \(2008\). Nature Cell Biology 10, 619 - 624.](#)



## TAME-DX Technology (Tumor Associated Microvesicle Enhanced Diagnostics):

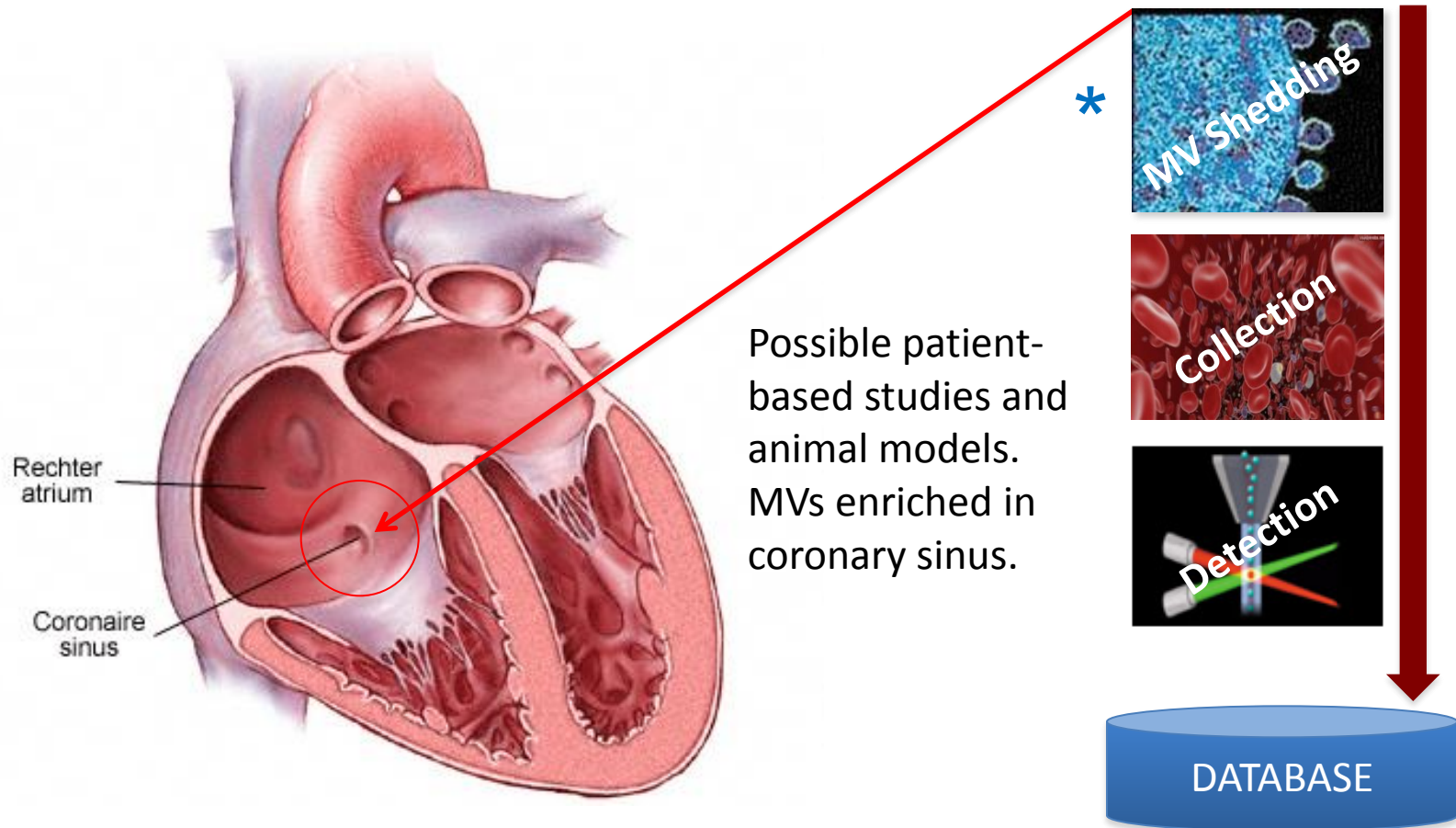
EGFRvIII in Blood Microvesicles – Rapid, specific, and early detection of brain tumor cells will permit early and tailored therapy, coupled to prognostic monitoring of patient progress. *(Reproduced with Permission of NX PharmaGen, Inc.)*



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# Translation of Microvesicle-Based Dx to the Heart



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# I know it was short – Here are some key summary points..

- Personalized medicine is maturing and will be a reality in the diagnosis, prognosis, and treatment of patients.
- From a complex interacting universe of biology will emerge new technologies accelerated to the clinic and bedside.
- The standard of care will change in parallel with new regulatory guidance to shape a new industry.
- *“The reality will lag behind the hype, but in the long run, genome information will have a transformative impact on [cardiovascular] research and practice”*. - Thomas P. Cappola and Kenneth Margulies, *Functional Genomics Applied to Cardiovascular Medicine* Circulation (In Press).