Universal Medica Group
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PRIZE 2011 INNOVATION Universal Biotech

Looking ahead: personalized medicine Biomarkers the necessary potential key partner for personalized medicine

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Heuristic systems biology

Innovation Days
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Biomarkers:
What do we speak about?

FDA definition:

A characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention (1999).

WHO definition:

Any parameter that can be used to measure an interaction between a biological system and an environment agent, which may be chemical, physical or biological (1993).

NIH definition:

A molecular indicator of a specific biological property; a biochemical feature or facet that can be used to measure the progress of disease or the effects of treatment (2002)

And all the others, ...

Biomarkers:
Same word multiple tools and usages.

- Biomarkers in Medicine
- Biomarkers in Early Drug Development
- Biomarkers in Drug Development & Decision Making
- Biomarkers in Clinical Trials & Studies
- Biomarkers as companion diagnostic before treatment
- Biomarkers in discovery
- Biomarkers for disease status before symptoms
- Biomarkers for treatment monitoring
- Biomarkers post treatment status

Why biomarkers?.

- Biomarkers are the roots of evidence-based medicine: who should be treated, how and with what.
- Without new markers, advances in better targeted therapies will be limited and treatments will remain largely empirical.
- Biomarkers development must be accelerated along with therapeutic developments.
- Biomarkers are the potential key partners for a successful personalized medicine

But what kind of biomarkers?

Biomarkers discovery.

The main questions attached to biomarkers concern
"robustness" and "objectivity".

The currently favoured approach:
High content screening & identification based on co-occurrences.

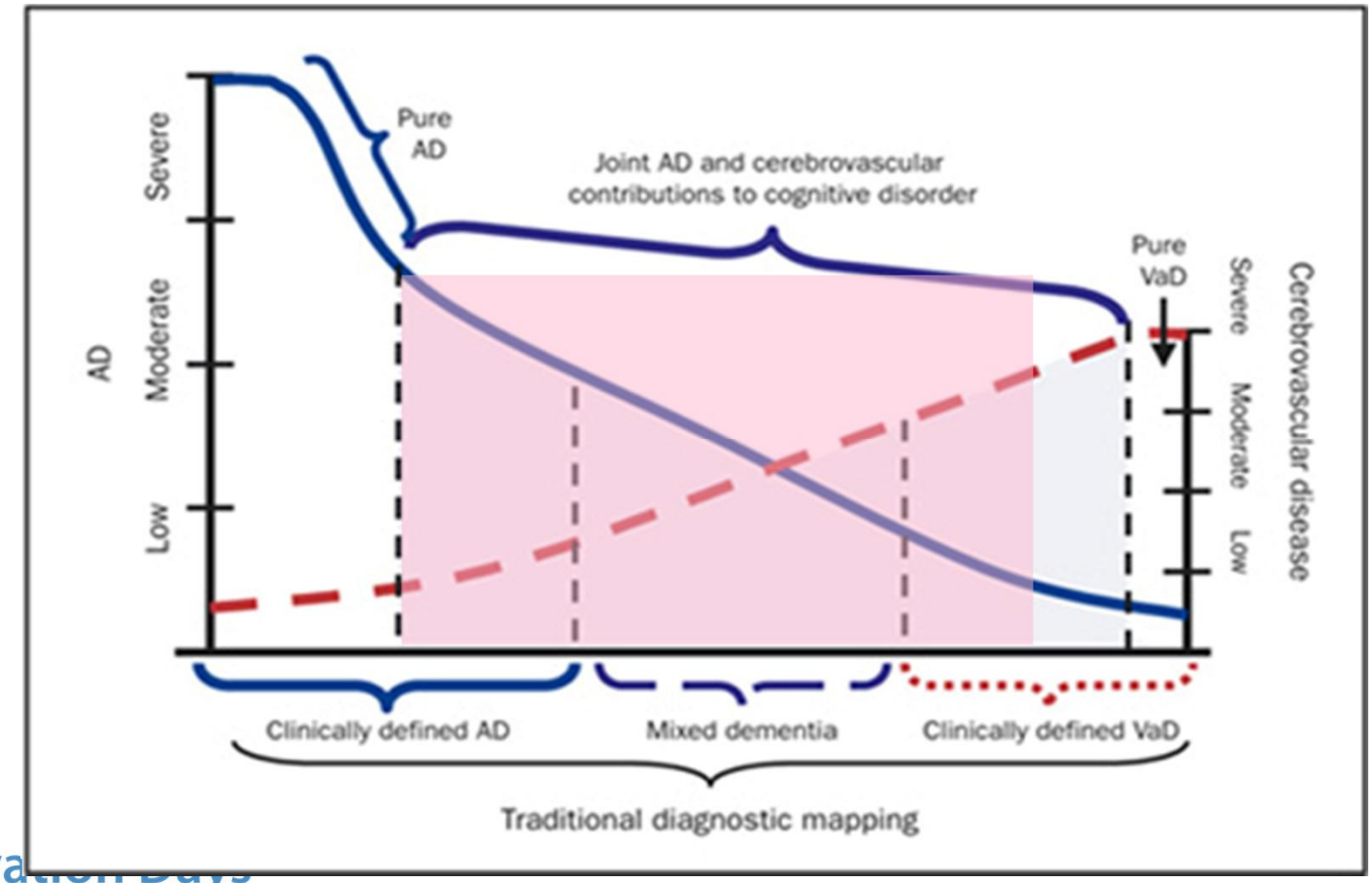
This can only identify "biomarkers" as a function of their
statistical occurrence and not their *physiological relevance*.

It also implicitly assumes a minimum level of clinical and / or therapeutic homogeneity.

That is certainly not the case for CNS pathologies!
They are highly heterogeneous in terms of symptoms, clinical presentation, disease progression and therapeutic responses.

Heterogeneous disorders

Syndrome-dominated thinking entirely clouds the issues. Diagnostic becomes a real problem (shaded pink area)



This issue, leads to sample misclassification.

Moreover, individuals affected by a severe disease often present a variety of concurrently induced/associated disorders, some of which remain under-diagnosed and their prevalence under-rated.

If it is accepted that a pathology must necessarily leave traces of its presence under the form of biomarkers, then the concurrent presence of another pathology, whether clinically recognised or not, must also necessarily do so.

What does this do to the problem of searching for *co-occurrences* between biological components *on the basis of serendipity* (the only possibility in the absence of pathophysiological understanding)?

Pertinent Biomarkers discovery

What relevance do biomarkers identified by statistical occurrence have for heterogonous CNS diseases?

How can conceptual & methodological problems be overcome to obtain physiologically relevant biomarkers?

How to escape?

To have the least chance of success, a knowledge of what to search for, where, when and why appears to be a necessity.

Adopting the wider views allowed by heuristic systems biology?
the concept of “pertinent” biomarkers: biomarkers related to a clear understanding of the mechanisms of the disease

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2011: CNS PSYCHIATRY: Pharmaco Psychiatry publication: Proteome-Based Pathway Modelling of Psychiatric Disorders. Publication with The max Planck Institute of Psychiatry in Munich. new analytical paradigm to definitively move research from “plethoric statistical biomarkers” to “targeted pertinent biomarkers” identification

Conclusions / Questions

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