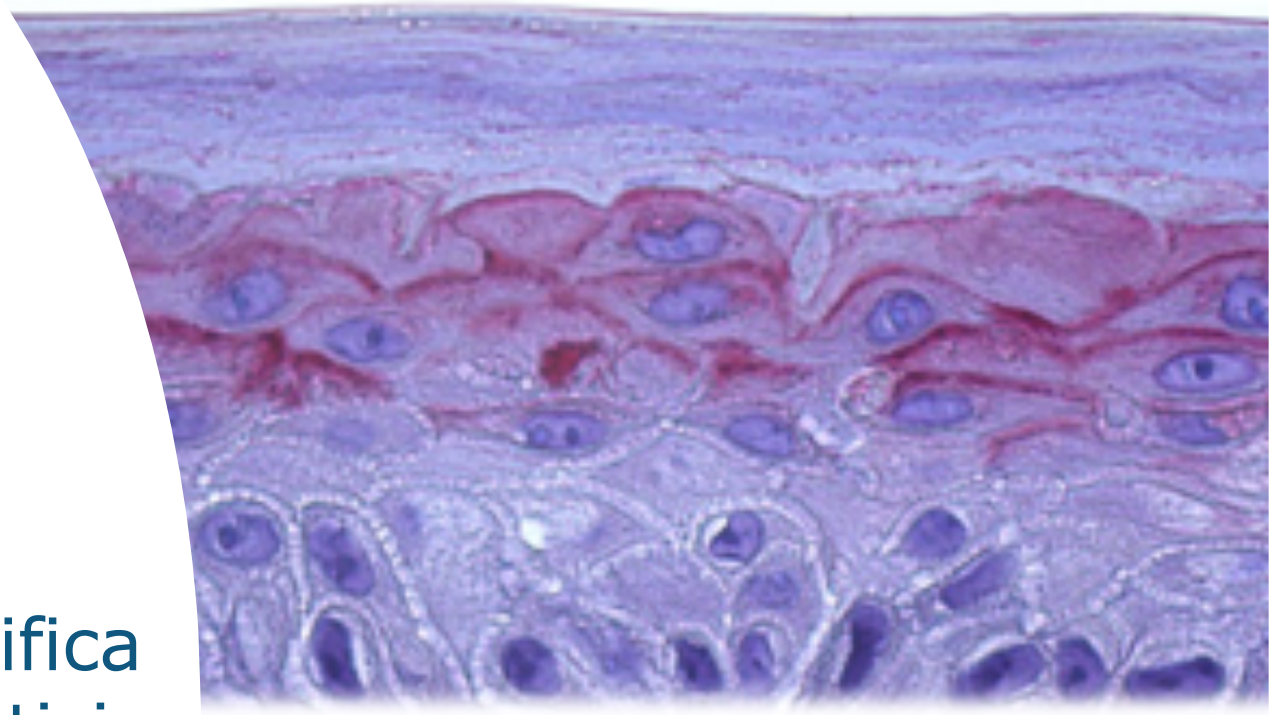
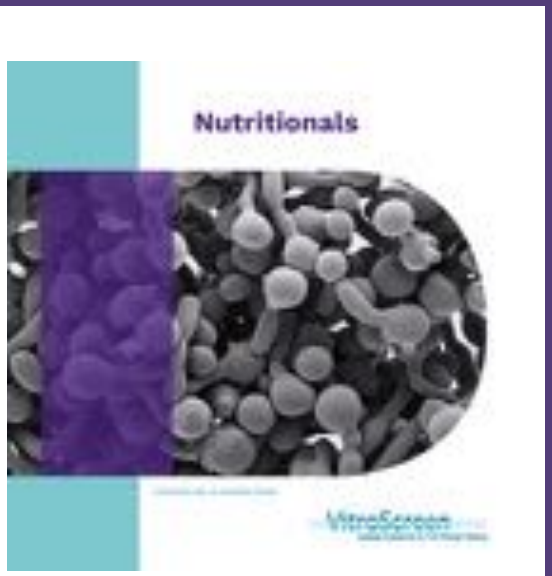
VitroScreen

Leading Innovation in Pre-Clinical Testing



I metodi per la verifica dell'efficacia dei cosmetici: presente e futuro delle valutazioni *in vitro*

Marisa Meloni,
Founder and CEO



PRE-CLINICAL EXPERTISE

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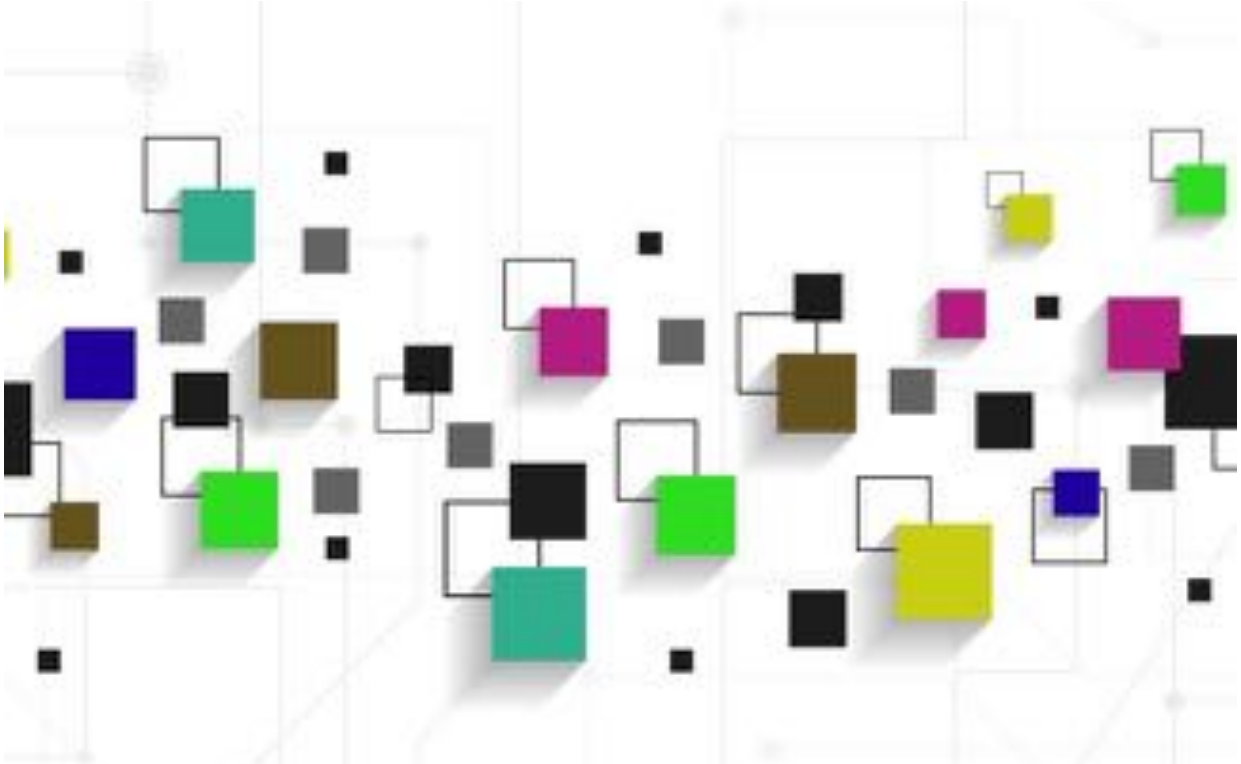
AGENDA



- DEFINIZIONI di Modello Sperimentale *in vitro* *e* di Metodo «Alternativo »
- VALUTAZIONI *in vitro* nel contesto della valutazione dell'efficacia pertinenza, robustezza, riproducibilità, eticità, valore e limiti nel supporto ai *claims*
- VALUTAZIONI precliniche del Futuro nel contesto delle Scienze della Vita

3.5.2 Performance assessment by ex-vivo methods

Products are tested in a controlled objective clinical study on volunteers and samples are extracted by minimal invasive methods (e.g. cells, suction blister samples, skin biopsies, D-Squames, skin lavage etc.).

The analysis of these samples (e.g. by biochemical, molecular biological, biophysical etc. methods) allows conclusions to be drawn on the actual effect of a product or ingredient topically applied in vivo.

The data generated from this type of tests can be classified as 'objective' with strong evidence of reproducibility if standardized and controlled conditions are applied.

The data can be used to support claims of product performance.

3.5.4 In Vitro tests:

These studies include

- simple biochemical assays without biological material as well as
- tests conducted using living components of an organism (e.g. cells, hair follicles, skin explants, reconstructed skin, etc.) that have been isolated from their usual biological surroundings.

These assays are typically conducted in laboratory ware (e.g. test tubes, flasks, petri dishes, microtiter plates, etc.) in order to perform all kinds of treatments and analysis under controlled test conditions **to provide the scientific proof for a specific biological efficacy, mechanism or mode of action of ingredients or formulas.**

The data generated from this type of test can be classified as 'objective' with strong evidence of reproducibility if standardized and controlled conditions are applied.

Protocols should refer to published or 'in house' validated methods.

FUNDAMENTALS OF COSMETIC CLAIMS

- Article 20 of the EC Cosmetic Products Regulation 1223/2009 (CPR) frames the requirements for cosmetic claims.
  Furthermore, cosmetic claims have to comply with EU Regulation 655/2013 that provides the Common Criteria to ensure **that the information conveyed to the end users through claims is useful, understandable and reliable so that consumers can make informed decisions.**

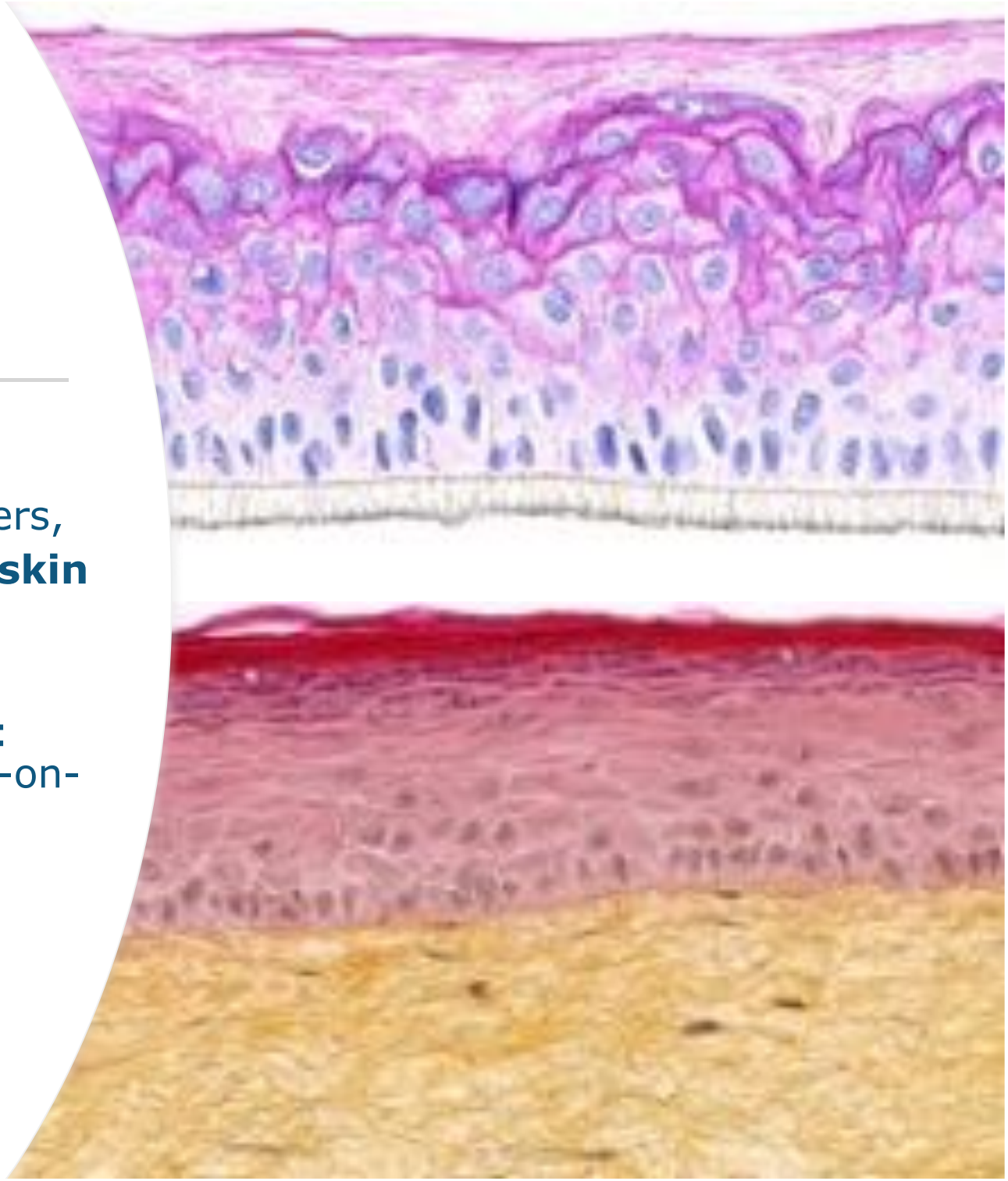
- The third Common Criterion, 'Evidential support', states that "claims for cosmetic products, whether explicit or implicit, **shall be supported by adequate and verifiable evidence regardless of the types of evidential support used to substantiate them, including where appropriate expert assessments**.

- Evidence for claim substantiation shall take into account state of the art practices. Where studies are being used as evidence, they shall be relevant to the product and to the benefit claimed, shall follow **well-designed, well-conducted methodologies (valid, reliable and reproducible) and shall respect ethical considerations."**

- **Experimental studies become a key instrument to substantiate cosmetic claims.**

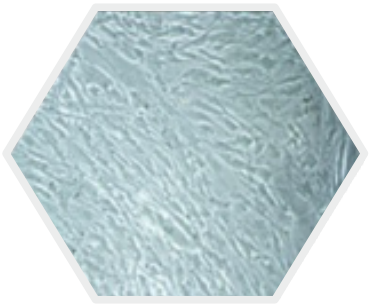
BIOLOGICAL SYSTEMS

- Bi-dimensional cell monolayers,
- **3D human reconstructed skin**
- Bio-printed tissues (?)
- *Ex vivo* explants
- Micro-Physiological Systems: spheroids, organoids, Organ-on-chip



INCREASING THE BIOLOGICAL RELEVANCE

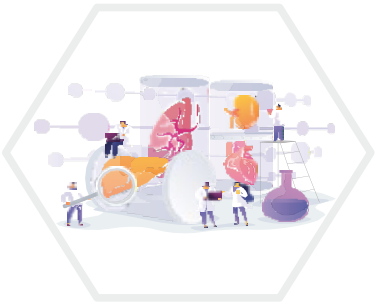
2D cell culture

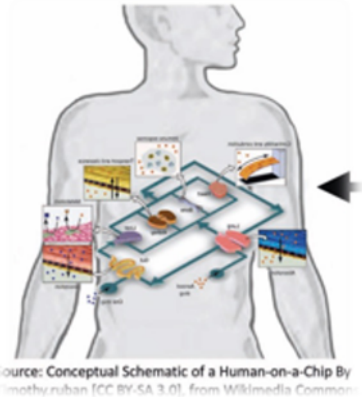


3D scaffold-free spheroids engineering

Dermopapilla

Miniaturized Organs





ource: Conceptual Schematic of a Human-on-a-Chip By

- Low functionality in a flat environment
- Low cell-matrix interactions
- No topographical guidance
- No mechano-trasduction and mechano-sensors
- Simplified molecular signalling and pathways
- No cellular dynamism
- Low molecular modulation and cellular polarization

- Biomimetic 3D tissue system
- High cell polarization
- Miniaturized model (⌀ 250-300 μm)
- 80% cell-cell and cell-ECM contacts
- 3D topographical guidance of endogenous ECM
- Multi-compartmentalization
- Homeostatic conditions
- Efficient endogenous ECM production
- 3D spatial distribution and organ-like functionality

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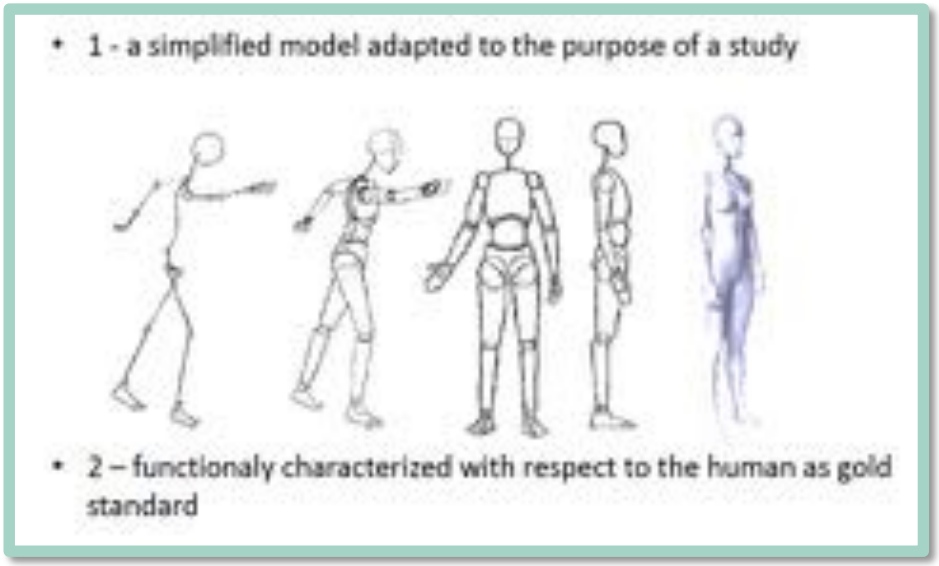
In vitro **EXPERIMENTAL MODEL** requires to be designed

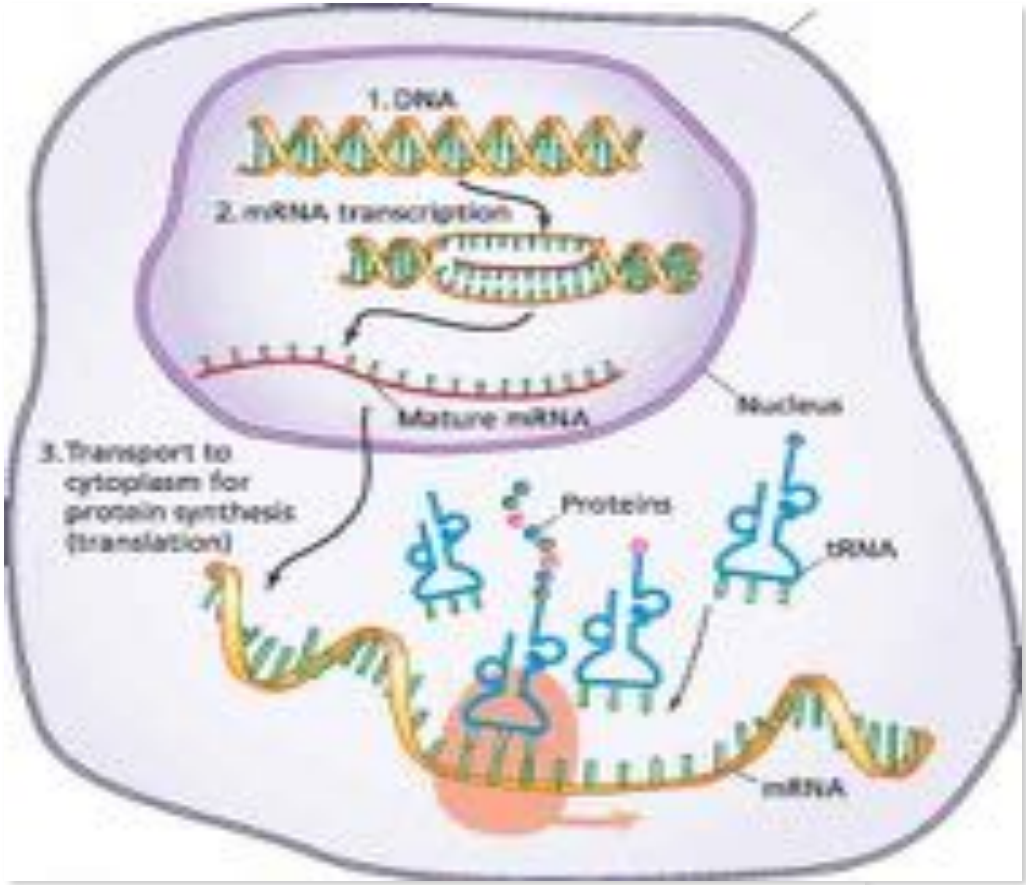


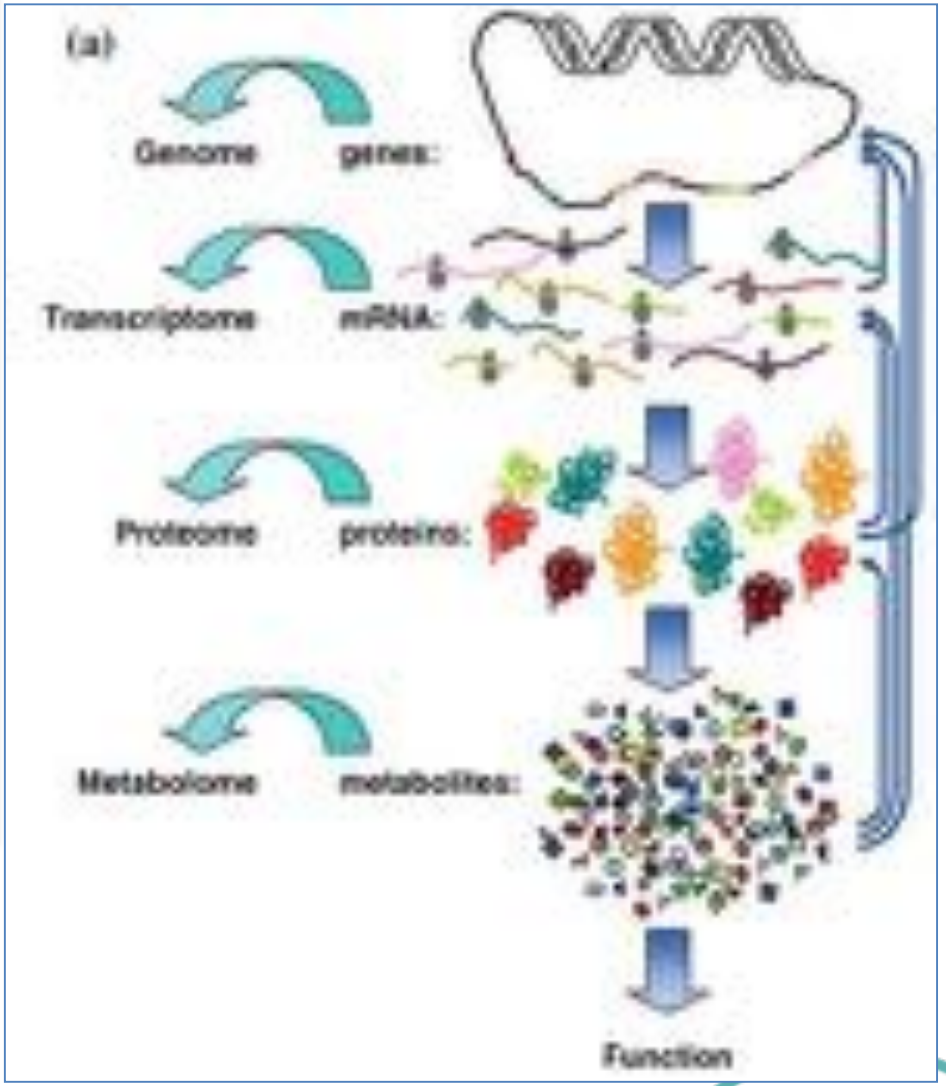
It is not a fast, cheap and simplified assay : it is based on a relevant biological system and aims to recapitulate morphological, functional and metabolic characteristics of a specific tissue or organ in physiological or disease conditions using a multiparametric approach
(possibly taking intoaccount dynamic).

«MUST HAVE»

1. Closer to human = **biologically and clinically Relevant**
2. Optimized to discriminate differences = **Reliable**
3. Developped to predict human response = **Predictive**
4. Can be repeated giving the same results = **Reproducible**
5. Optimized to investigate the more relevant parameters = **Robust**
6. Reference molecules, positive negative controls **must be** included

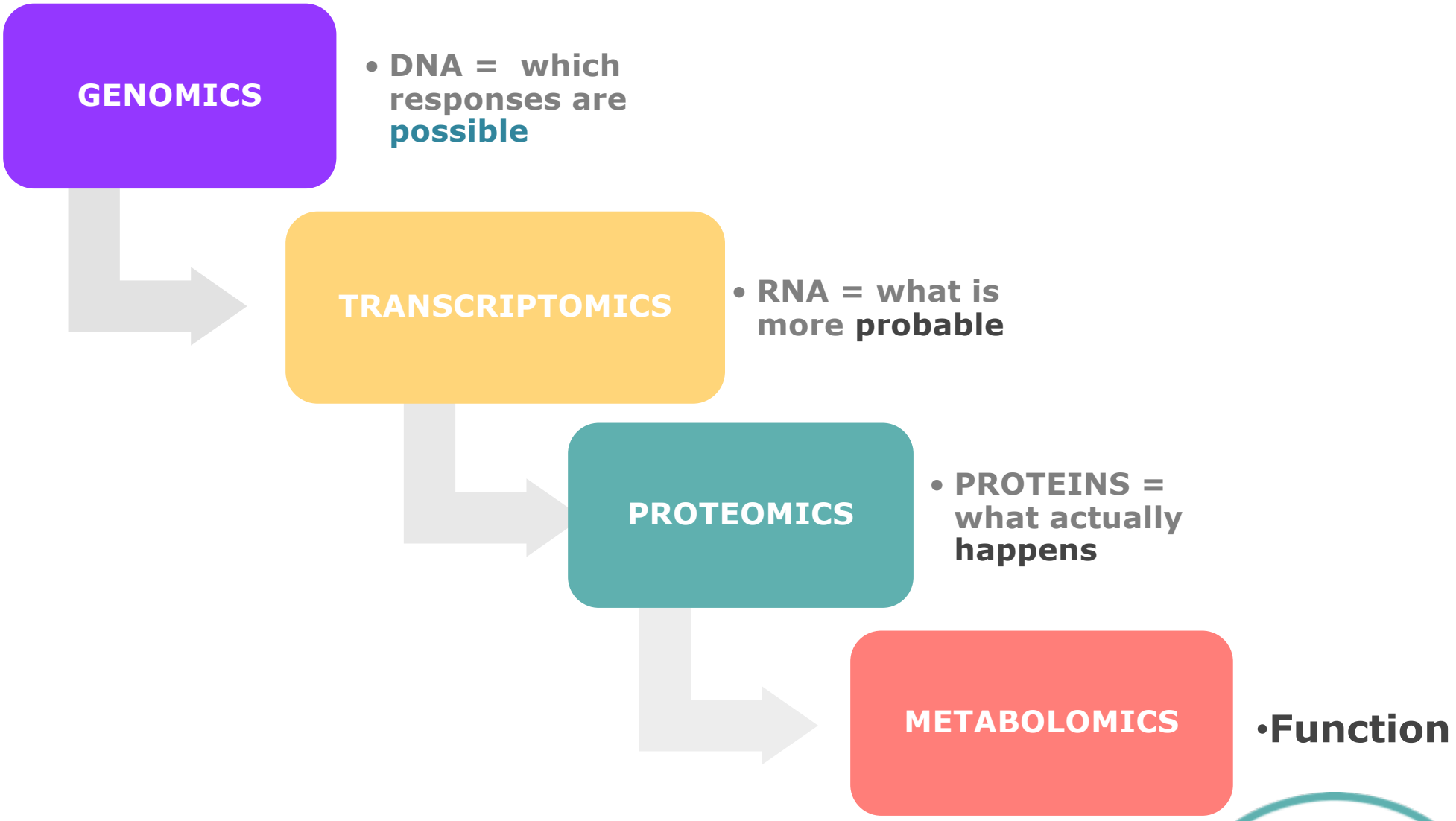
CRICK'S CENTRAL DOGMA: MOLECULAR BIOLOGY



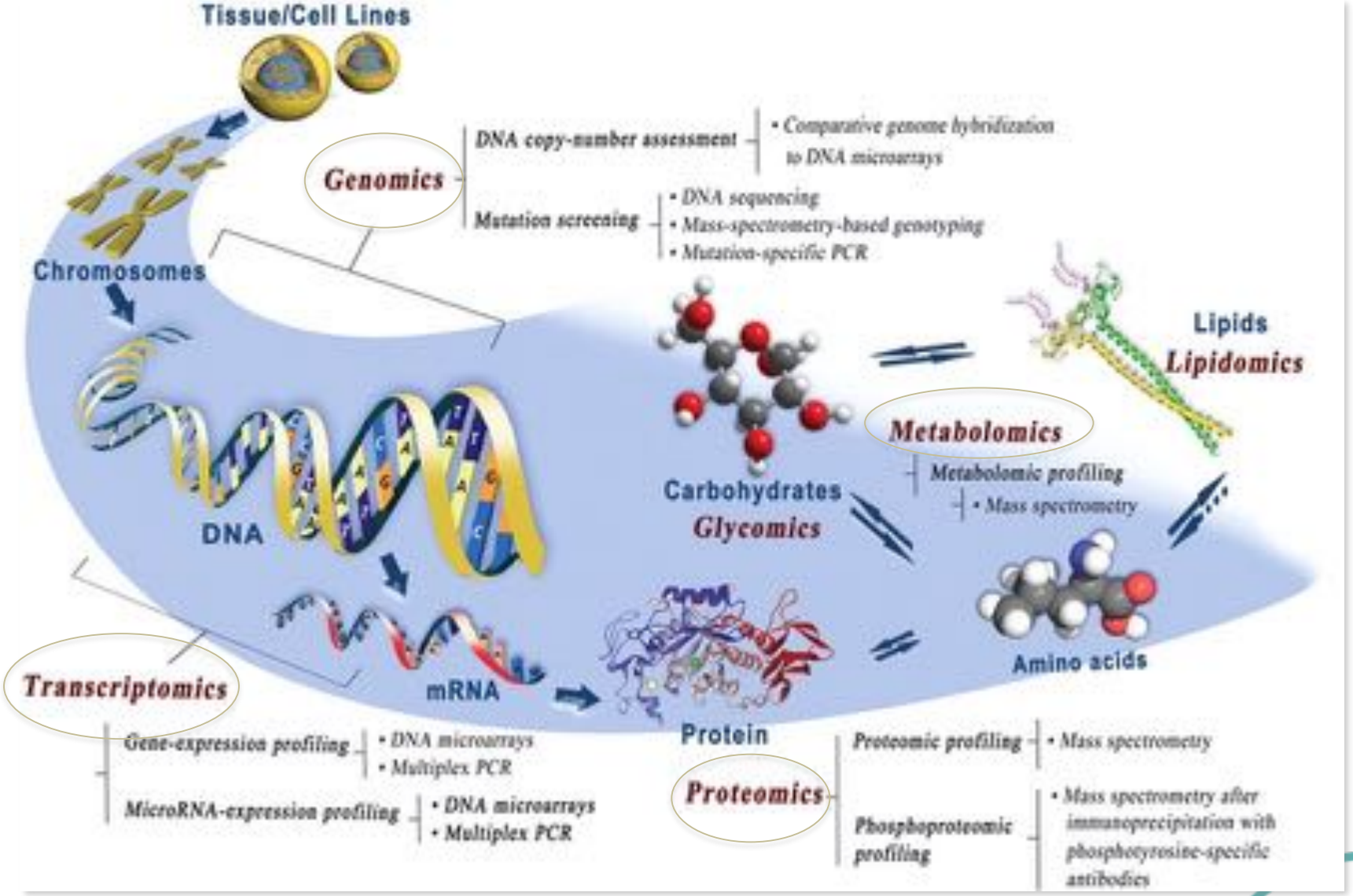


At the hearth of the cell the DNA acts as a Director of countless pathways and biological functions.

‘OMICS LANGUAGE’



'OMICS: TECHNIQUES



ADVANTAGES *in vitro* Experimental models

L'ARTE DI METTERE ORDINE
URSUS WEHRLI

Clinical data *Biological mechanisms*

- To provide the **mechanism of action** based on robust **scientific evidences** that cannot be obtained with clinical approaches, either for practical or ethical reasons
- **Ethical** when the parameter to be investigated is invasive/stressfull for human volunteers or can induce a damage (UV exposure, photosensitization..)
- **Unique approach** when the parameter cannot be explored on volunteers in a defined experimental window (photoageing, oxidative stress damages) with the power to inspire or being complementary to clinical evaluation
- Added value to R&D Innovation efforts and powerfull in direct and indirect scientific communication
- Key tool during R&D: to perform actives and formulations screening with reproducible results during product development
- **LIMITS**: biological relevance of the test systems, scientific value and pertinency of the models and how they are **used** to substantiate the claims

NAMS IN SCIENCE AND REGULATIONS

EURL ECVAM status report describes EU funded research projects, validation activities and other initiatives that promote the uptake and use of NAMs in science and regulation.

….***Shifting*** *to next generation animal-free approaches does not mean less protection for humans and the environment. It rather promises a move* ***from assessments based primarily on observations and extrapolation to those based on better understanding of biological processes and their alterations****, ultimately providing levels of protection to humans and the environment that are at least as good if not better than those provided by animal tests.*

NAMs should therefore be seen as an opportunity to avoid ethical dilemmas and scientific inadequacies involved in routine regulatory testing in animals.

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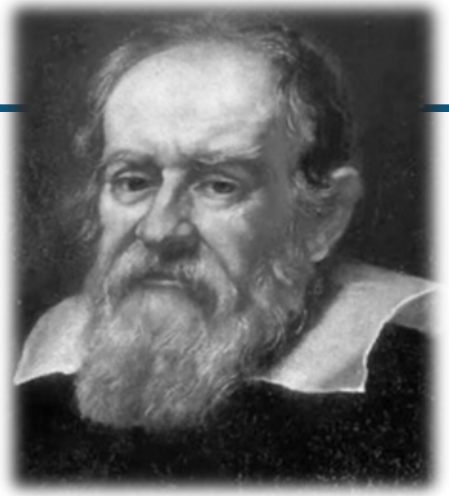
QUID MENSURA MENSURATUR
UT QUOD NON MENSURATUR

"Misura quello che è misurabile e rendi misurabile ciò che non lo è"

Galileo Galilei,1564-1642



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Grazie !