

## What are the different types of biochips ?

The "microarray" term goes up to about thirty years with the "Southern Blot" technology introduction by professor Edwin Southern describing the labelled DNA molecules use to question by hybridization the DNA molecules linked to a solid support. However, this approach only uses one gene at the same time.

When the scientist took up the challenge of the whole human genome sequencing ("Human Genome Project"), it raised a challenge even larger: It's to understand the genes functions which make our genome. For that, it was necessary to detect the gene expression levels according to various conditions, so as to accelerate the identification of the targets associated with the diseases and to develop new diagnosis and therapies.

Thus, the first "arrays", (meaning "ordered row") based on the principles evoked by Southern, appeared to meet the needs to analyze in parallel the form of multiple genes.

The term of "**DNA arrays**" is generic. Initially, conceived for nylon porous membranes (called "macroarrays" in opposition to "microarrays") which imposes a radioactive marking, difficult to employ and allows the observation only few hundreds of genes at the same time.

At the end of the Nineties, the "DNA arrays" were gradually developed on glass slides where thousands of DNA fragments can be deposited by robotized processes. Thus, the miniaturization, made possible by the use of a solid support, fluorescent markers and by progress of robotics, allows to manufacture high density chips, which cover the integrality of an organism genome on a simple microscope slide.

The passage of the "DNA arrays" to the "**Protein arrays**" seems a logical continuation.

Nevertheless, reality is different owing to the fact that the protein structures and functions are more complex than those of DNA and less stable. Moreover, each type of cells contains thousands of different proteins and some are specific of a cellular type. Also, the protein profile varies with the age and the environmental conditions.

The term of "chip" concerning proteins is extended to systems having a size scale higher than the standard size of the DNA chips and densities much weaker (a few tens to

a few hundreds of spots). In the same way, microarrays where capture agent corresponds to nucleic acids (aptamers) making it possible to detect proteins will be also considered.

Though the manufacture does not have major differences, we can schematically classify the "protein arrays" in two categories according to their uses: "capture microarrays" to detect and quantify a specific protein like protein markers of tumors and "functional microarrays" where more complex parameters are analyzed: functional activities (enzymatic), characteristic of the interactions (affinity etc...) with varied partners.

The "**tissue arrays**" allow the thousands of tissue samples analysis on the same glass slide. They start to be used to detect the protein profiles on healthy and sick tissues and to validate the potential of target drugs.

The "**cell arrays**" accelerate considerably the study of unknown function genes and their potential implications in various diseases by analyzing the phenotypes resulting from an excess or the temporary protein extinction in the small cell islands. This array format seems also particularly interesting for the high throughput screening of active principles or pharmacological molecules. The manufacture of these "cell arrays" requires to perform opposite and simultaneous transfections of several thousands of different nucleic acids on the chip. This new technique has the advantage of allowing a parallelism quite higher than the microtitration plates, to decrease work volumes by miniaturization, appreciable when we use rare cells (stem cells) or expensive reagents as the siRNA (shorts interfering RNA which allows the gene expression extinction) resulting from chemical synthesis.

The "**chemical microarrays**" are arrays made up of small organic molecules, peptides or sugars. Thus, the pharmaceutical companies can simultaneously screen tens of thousands of potential drugs candidates.

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