

Comparative genomics of nuclear hormone receptors

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Background and objectives

Data relative to biological sequences accumulate not only in exponentially increasing quantities, but also in increasingly heterogeneous data types: genomic or genic sequences, 3D protein structures, expression patterns, alternative splicings, biochemical (enzyme, receptor, etc) or physiological (homeostasis, reproduction) function, protein-protein interactions, medical implication, etc. At present, each of these data is stored separately, in different formats, hugely complicating crossed queries or information exchanges. Moreover, these data have often been determined with different resolutions, in different model organisms, with different experimental approaches. The aim of the project was to focus on a gene family which is very important as a therapeutic target in farm animals as in human: nuclear hormone receptors. The project was focussed on four model organisms (bovine, chicken, pig and zebrafish) and to: (i) complete existing data on expression patterns of these genes, notably in the chicken where little is known of these patterns; (ii) establish a database allowing simultaneous representation of different types of data in a structured manner, notably expression patterns experimentally determined (zebrafish, chicken, mouse) or derived from EST data (bovine, pig, chicken, mouse, rat, human).

Results

The results we obtained can be summarized in three main points: (i) we completed the determination and analysis of NR expression patterns (plus 30 of their main coregulators) in zebrafish (Bertrand et al., in press). In addition we cloned all NR genes in chicken and started the study of their expression pattern during development. (ii) We extended Nurebase, a specific database devoted to NRs in order to include gene expression data based on ESTs as well as structural and pharmacological data. NurXbase, the new version of the base, fused to a structure-oriented database maintained at Illkirch will be soon available on line. (iii) Given the new possibilities offered by the extensive number of global analysis of expression patterns, we extended our gene expression database project to all genes. We are developing an ontology and specific tools to allow efficient expression pattern comparison and analysis. This extended database is now developed in close collaboration with Marc Robinson laboratory at Lausanne University.

Conclusion and perspectives

The NR gene family, given the extensive and diverse knowledge accumulated because of its interest in human and animal health proved to be an excellent model to allow integrative approaches at the genomic scale.

List of the publications:

- 1 S. Bertrand, B. Thisse, R. Tavares, L. Sachs, A. Chaumot, P-L. Bardet, H. Escriva, M. Duffraisse, O. Marchand, R Safi, C. Thisse et V. Laudet Unexpected Novel Relational Links Uncovered by Extensive Developmental Profiling of Nuclear Receptor Expression **PLOS Genetics**, *in press*
- 2 E. Ribes, J-M. Wurtz, E. Lo Piparo, G. Parmentier, M. Robinson-Rechavi, J-P. Cravedi, D. Moras, E. Benfenatti et V. Laudet NureXbase : An extension of Nurebase, a specialized database for nuclear receptors *in preparation*