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MAIN RESEARCH INTERESTS

I'm interested in understanding and predicting the relationships between the sequences, structures and functions of proteins, the evolutionary conservation of these features and their alterations upon mutations leading to diseases. To that aim, I develop original methodologies for sequence analysis, especially based on the HCA approach (see below). Together with other tools, these help revealing information into yet unexplored areas of computational biology. These are applied to the evolutionary analysis of protein domains and protein architectures, with a special interest in the analysis of orphan protein domains and in the discovery of new families of domains, which are not yet described. Topology-based methodologies are also developed to address fundamental issues about protein folding and protein interaction properties.

SOME RESEARCH TOPICS

• Identification of novel families of domains

HCA has been used in combination with current bioinformatics tools to identify novel families of domains (or significantly extend some other ones), especially starting from the analysis of orphan sequences.
BRCT (Pubmed, Smart), TUDOR (Pubmed, Smart), BAH (PubMed, Smart), LEM (PubMed, Smart), FERM (PubMed, Smart), RUN (Pubmed, Smart), dDEEN/DENN/uDENN (Pubmed, Smart), EMI (PubMed, Pfam), HYR (PubMed, Pfam), Beta-CASP (PubMed, Smart), OCRE (PubMed), ZP-N (PubMed), LOTUS (PubMed), PWAPA (PubMed), REPULS (PubMed), Harmonin (PubMed), SRI (PubMed), ...

• Proteins involved in diseases

We are frequently involved in the analysis of proteins, in which mutations are associated with the development of inherited diseases.
Proteins involved in immune system diseases are especially considered, in collaboration with members of the Imagine Institute (genome dynamics (PubMed), cytotoxic activity of lymphocytes (PubMed), ...), as well as proteins involved in hormone metabolism (PubMed). A special emphasis is also given to membrane proteins, such as members of the ABC superfamily (CFTR (Cystic Fibrosis) (PubMed), ABCB4, ...) and ferroportin (hemochromatosis) (PubMed)). In the field of cancer research, the aim of our AMMABIO group is especially to understand the cellular response to DNA damage and telomere regulation, as well as the molecular mechanisms involved in the radiation-induced DNA damage. We are also interested in proteins involved in infectious diseases (parasites (PubMed), viruses).

• Evolution of genes involved in specific functions

We are also interested in understanding the evolutionary processes associated with specific functions, in collaboration with teams studying reproductive systems (PubMed) and telomere regulation (PubMed).

HYDROPHOBIC CLUSTER ANALYSIS (HCA)

Hydrophobic Cluster Analysis (HCA) has been developed in the late 80's, under Jean-Paul Mornon's inspiration. It is a useful tool to analyze protein sequences in light of the structural invariants of protein folds, especially «orphan » sequences for which no information can be readily obtained through current bioinformatics tools. Based on this approach, tools have recently been develop to predict foldable domains from sequences and help to analyze orphan sequences. We are also developing methodologies for predicting hydrophobic features of interaction sites. The developed tool, used together with available evolutionary methods, will be applied in our AMMABIO group to the analysis of large macromolecular complexes obtained by cryo-electron microscopy.

Guidelines to the use of the method and references (methodology, applications) can be found here

Some HCA-related tools :

• DrawHCA: HCA plots.
• Cluster code converter: Conversion of a binary code to a Peitsch code (decimal integer) (Leduc et al., unpublished data).
• Hydrophobic Cluster dictionary: Secondary structure propensities of the most frequent hydrophobic clusters (Eudes et al. BMC Struct Biol 2007).
• SEG-HCA: Predicts foldable segments within protein sequences (Faure and Callebaut PLOS Comp Biol 2013).
• TREMOLO-HCA: Adds to sequence similarity searches information on domain architecture and on conservation of core-forming amino acids (Faure and Callebaut Bioinformatics 2013).

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