LightDock [3] is a multiscale flexible approach for the 3D determination of protein complexes based on the Glowworm Swarm Optimization (GSO) algorithm [4] that systematically optimizes the generated docking poses towards those energetically more favourable at every simulation step, agnostic of the force-field. We present a novel two-step method for including interface residue restraints in protein docking simulations which has been implemented in the LightDock protocol. Prior to the simulation, irrelevant regions are excluded for sampling (filter of initial swarms) and initial ligand poses are pre-oriented towards the interesting local regions defined by the information provided. Additionally, the restraints information can be also taken into account in the scoring depending on the scenario.
This new method has been benchmarked in the new 55 cases of the Protein-Protein Docking Benchmark 5 [5] (assessed according to CAPRI criteria [6]) over different scenarios varying on the amount of information used and with special emphasis on antibody-antigen cases, where restraints from the CDR loops could be easily extracted beforehand. The excellent performance obtained, even with fuzzy information, demonstrates its direct applicability in real-case scenarios with diverse experimental information.

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G04-08-P85 F,M

Exploiting metabolic gene expression for prostate cancer stratification

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Metabolic changes are central to cellular transformation and cancer progression. We have contributed to demonstrate that this metabolic rewiring is orchestrated by master regulators that act through the regulation of transcriptional programs. In this line, the transcriptional co-activator PGC1α suppresses prostate cancer progression and metastasis through the activation of estrogen-related receptor alpha (ERRα) [1]. Furthermore, we showed that a manually curated geneset based on the combined activity of PGC1α and ERRα exhbitied prognostic potential in barios prostate cancer datasets [2,3,4]. Based on these encouraging results, we pursued 2 clinical objectives: 1) to refine the prognostic signature based on PGC1α and ERRα activity and 2) to explore the prognostic capacity of the metabolic transcriptome as a whole. To this end, we took advantage of genetic algorthims that provide an unbiased strategy for the generation of gene signatures. Both strategies yielded highly prognostic gene signatures that were predominantly selective of prostate cancer. Importantly, hazard ratio or negative predictive value using as endpoint biochemical recurrence provided distinct signatures with specific clinical applications. Finally, thanks to these approaches we were able to stablish a list of genes potentially responsible for prostate cancer aggressiveness, which biological study could expand the metabolic bases of cancer progression.

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G04-09-P86

Computational analyses of sumoylation in protein kinases: a biomedical perspective

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Sumoylation is a general post-translational modification that regulates several cell processes such cell cycle control, transcription, DNA repair, and chromosome segregation. It is a covalent attachment of a small ubiquitin like modifier SUMO protein to target protein lysines. This attachment affects biological functions of target proteins by blocking interactions sites, creating novel sites, or inducing conformational changes. Some kinases are regulated by this mechanism. For instance, AuroraB kinase, MEK, FAK and ERK5 are known targets of sumoylation. Give the importance of kinases as a main player in signal transduction processes, as well as being very relevant to disease and development, we aimed to address whether this mechanism is anecdotal or general within the kinase superfamily, and also if there are over-represented in developmental pathways. To this purpose, we set to identify suitable features from these proteins that could be associated to infer and predict the impact of SUMOylation. Using bioinformatic/computational approaches we have 1) analysed potential SUMOylation in kinases subfamilies, 2) analysed them according to structural constraints, and 3) estimating its presence in cancer samples that exhibit different mutation rate, and 3)mapping SUMOylation distributions in kinases involved in developmental pathways. Our results demonstrate that protein kinases could be highly regulated at both family and superfamily level, where potential sumoylated lysines are significantly distributed close to active sites, away from binding sites, and interestingly buried within the protein. We have not found any significant presence of SUMOylable lysines in cancer, so according to our data, SUMOylation alteration may not be a general mechanism contributing to cancer development in the Kinase superfamily.
Keywords: Computational Biology, Sumoylation, Protein kinases, Bioinformatics, Disease, Cancer, Python/R.

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G05. Chemical Biology

G05-01-OI

Mechanisms of tissue-specific and time-dependent metastasis

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Although breast cancer (BCa) can relapse to bones, lungs and liver as well as brain, metastasis frequently becomes prevalent in