

Immunometabolic effects of vitamin D unravelled by an integrative systems biology analysis

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Valorization

Science research as a collaborative network

One of the milestones in bioscience research is the generation of a wide variety of large scale databases that compile very specific information related to molecular biology. Nevertheless, for the correct management of this bulk of data, the science community has established the FAIR basic features of data management which allow their correct usage. First, data must be referenced using identifiers or attributes that are findable in other sources. Secondly, data has to be accessible to everyone in the science community, therefore the platforms and databases containing this information have to be open and a science-based community has to ensure its routinely curation and update. Furthermore, the format of the data has to be interoperable, ensuring that the structure of the data is compatible and suitable with the standard tools of the science community. Finally, the way data and its metadata is stored and written must ease its replication and combination with other features.

The usage of these public repositories that contain datasets and databases from wet-lab experiments should be a crucial part of every research project as we demonstrate in this thesis. Accessible public data from other researchers allows the possibility to exploit it with bioinformatic tools for the purpose to try to explore biology aspects that the authors have not considered in their original hypothesis or to compare/combine it with other data sets to obtain more robust evaluations. Furthermore, a great feature of this bioinformatic pipeline built in this project (**Chapter 2**), it is possible to process several dataset that share a common pattern (e.g. different cell models with same treatment) allowing their comparison and plotting the results in a friendly way that makes possible a better understanding of how a specific biology system works. Exploiting public data from other researchers and interpreting the results at different molecular biology levels gives a rich and wide insight that is crucial for the first step of a new project: hypothesis establishment. Finally, the re-use and re-analysis of data allows the discovery of new aspects that were not considered in the original approach; as a result its quality and, in consequence, its value increase.

As mentioned above, generation, storage and analysis of public data are crucial for every project in its first steps; but it is worth mentioning the importance of the actual researcher-researcher interactions from different science fields to have a wider outlook of the system of study. Collaboration between different departments that are specialized in specific niches in science allows the usage of a variety of techniques optimizing the work and time invested in research to validate a hypothesis (**Chapter 2**). This gap that separates bioinformatics and wet-lab research, is closing bit after bit with the initiative of this kind of collaborative project. Most importantly, young researchers working and being trained in different niches in science widen their perspective, easing their adaptability in further research projects. The joint project that formed the basis for this thesis is a great example of how a good collaboration between departments with different focus and methods at two Universities can result in an interesting, novel and rich study on a very specific aspect of biology and, in consequence, generating data that with high quality and value.

Future perspective: optimizing cell therapy

The tolerogenic dendritic cell population that we have focused on in this project are crucial for the immune tolerance homeostasis. Disruption in the regulation of the immune tolerance of the individual can lead to anomalies that are known as autoimmune diseases that are characterized by the attack of the host immune system to self components. The immune system has developed mechanisms to avoid these pathologies such as processes to remove immune cells that recognize self-antigens and would provoke an auto-attack. Finally, the immune system also is capable to develop specific cells that inhibit self-reactions processes known as regulatory cells which include the ones focused on this work: tolerogenic DC and T regulatory cells.

The results of our work gave a better understanding of how vitamin D modulates the development of tolerogenic DC based on a metabolic reprogramming. The findings presented in this thesis describe how shifts in metabolism induce changes in the immune function of tolerogenic DC and, in consequence, affect Treg development. This contributes to the notion that immuno-metabolism is an emerging aspect of biochemistry that needs better understanding to explain that key metabolic pathways are essential for the correct execution of immune actions. Decryption of the links between metabolism and immune cell fate can lead to the optimization of cell culture for the generation of specific cell populations that can be used to treat and cure diseases. In that way, this kind of findings can improve personalized cell therapy.

Promoting multi-disciplined professional researchers

The bioscience field is living a constant evolution where computation and data management are taking important roles for its progress. These new dry-lab tools have found a niche in bioscience known as bioinformatics but more bridges have to be built to connect this field to the different wet-lab niches, and this thesis is one example of that. As a PhD student, working in these two different science fields has granted me the opportunity to enrich me as a researcher from many different perspectives as well as meeting numerous professionals from both sides. Science progresses in higher levels when its community works as a network where different scientific areas complement each other; optimizing time, work, resources and, in consequence, results.

The community within the University has to keep ensuring the acquisition of multi-disciplined skills to students that will be involved in different fields of science. In computational science, there is a large variety of bioinformatic workflow tools that are crucial for bioscience research that optimize their performance and the quality of the work. That is why knowledge of basic programming languages is important in a professional research career which guarantees the efficiency of work performance in a science project. My personal experience taken from this collaborative project has proven that the integration of skills and knowledge from different fields is an investment that in the long term is very profitable for Universities since it guarantees valid academic professionals that can work in very competitive research projects.