Proyecto PID2022-137615OB-I00 financiado por MCIN/AEI/10.13039/501100011033/ y por FEDER Una manera de hacer Europa

Identificación del proyecto:

Caracterización completa de las inversiones polimórficas humanas mediante datos de secuencia de lecturas largas

Descripción del proyecto:

This project is focused on the study of genome variation and its role in phenotypic diversity, which has interest both for basic science and human health. During the last years, the intense effort and the technological advances are finally setting the basis to identify all human genetic variants, including both SNPs and small indels and larger structural variants (SVs). However, many complex SVs are still not well resolved and accurate genotyping data in multiple individuals are needed to determine their real consequences. Inversions are one type of SVs that affects a large fraction of the human genome and is implicated in phenotypic differences between individuals in diverse organisms. Nevertheless, due to the difficulty of their detection, inversions mediated by inverted repeats (IRs) are still poorly studied and many of them have appeared recurrently multiple times in humans and in other species. Interestingly, inversions are quite unique in their effect of recombination and the associated fertility costs, which makes that they can have a higher functional impact than other variants. Therefore, we plan to combine the knowledge generated about inversions with the newest genomic information and innovative techniques to finalize the analysis of these elusive variants. The main goals are: (1) Complete the catalogue of the full spectrum of human polymorphic inversions and their breakpoints; (2) Develop new genotyping and imputation assays based on long read information to characterize missing inversions in large population datasets; (3) Carry out an integrative analysis of the functional effects and the association with phenotypic traits and disease susceptibility of the newly characterized inversions; (4) Obtain a global estimate of the inversion mutation and mosaicism rates in humans from the available long-read data; and (5) Do a genome-wide analysis of IR conservation and inversion recurrence taking advantage of new long-read mammal genome assemblies. The proposed research represents a key step forward in the complete characterization of one important type of variation, that could serve as an example for other SVs and contribute to fulfill precision medicine promises. Moreover, it would help us understand better how these changes are generated at different levels, from somatic cells to evolution, and the possible functional implications of inversion recurrence.

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