XY-CANGEN: Deciphering the role of biological sex in cancer genetics

Description

Over the last decade we have made significant progress in understanding the role of genetics in cancer predisposition, evolution andtreatment. We now have thousands of germline variants associated with different types of cancer and we have also identified a fewhundred genes that, when somatically mutated, drive the growth of cancer cells.However, there are also many open questions to which we do not have, yet, a conclusive answer, and some of the most pressing oneshave to do with the role of biological sex in cancer. For example, we know that the incidence of multiple cancer types (thyroid, pancreas,brain or bladder, among many others) is significantly different in males and females, sometimes by orders of magnitude! Similarly, cancergenes have different somatic mutation rates depending on the sex of the patient. Last, but not least, many cancer drugs work differently inmen than in women.In XY-CANGEN, we propose to study the role of biological sex in cancer genetics. To that end, we will use large cancer geneticsdatabases (Objective 1), with over one million individuals, to identify germline variants that predispose to cancer in different ways in menand in women (Objective 2). Then, we will do the first comprehensive study of germline cancer variants in chromosome X, which, so far,has been excluded from the majority of cancer GWAS (Objective 3). Next, we will test whether all these germline variants with sex-specificeffects are interacting with cancer driver mutations (Objective 4). Finally, we will use our website, Cancer3D, to present all the results ofXY-CANGEN to the cancer research community, allowing them to move our results forward.In conclusion, we will do the first comprehensive study of the role of biological sex in cancer genetics. The results of this project could haveimplications for cancer prevention and early detection (for example, by adapting polygenic risk scores to the sex of the patient), as well astreatment.

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