Structural insights into T-cell receptor interactions with p53 neoantigen to improve the adoptive cell therapy

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INTRODUCTION

The role of p53 in the biology of mammary epithelial stem cells is well established. may counteract stem cells expansion by several mechanisms, including restriction of self-renewing divisions and block of reprogramming of somatic/progenitor cells into stem cells.p53 regulates the polarity of cell division in mammary stem cells. p53 is often inactivated by loss or mutation in breast cancer. This inactivation favors symmetric divisions of cancer stem cells, contributing to tumor growth.Two recent studies demonstrate an unexpected link between p53 and stem cell biology that include a metabolic pathway, the mevalonate pathway.

Cancer is one of the most dreaded diseases of the 20th century and spreading further with continuance and increasing incidence in the 21st century. The situation is so alarming that every fourth person is having a lifetime risk of cancer. India registers more than 11 lakh new cases of cancer every year, whereas, this figure is above 14 million worldwide.

Cancer cells continue to grow unless one of four things occur: (1) The cancerous mass is removed surgically; (2) using chemotherapy or another type of cancer-specific medication, such as hormonal therapy; (3) using radiation therapy; or (4) the cancer cells shrink and disappear on their own.

EXPERIMENTALS

The terms which were referred to in PDB (protein data bank) search box are stem cells in cancer. As per the subject there are 1,71,310 results. As of further analysis of the structure, furthermore refinement has done by selecting more options, finally P-53 Specific T Cell Receptor with PDB ID 6VTC has been selected. (figure 1)

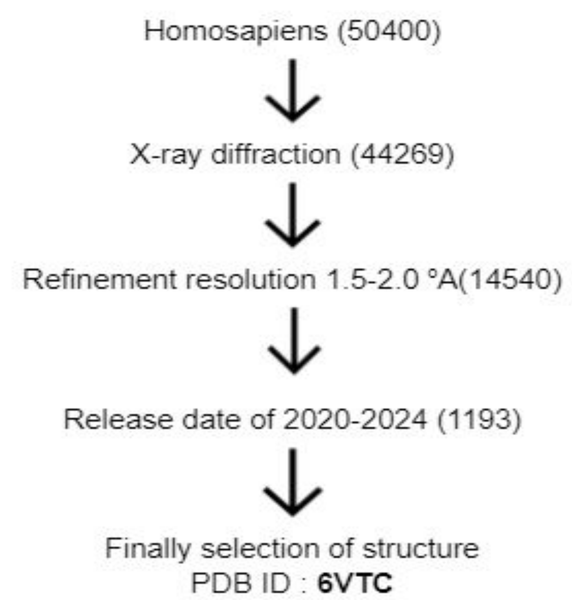

figure 1 - selection of structure using PDB

To test whether the structure is good quality we do the following two tests

1. R-work is less than 1/10th of resolution
2. The difference between R-Free & R-Work 0.041 which is less than 0.05
   According to the above values the results says it was a good structure

For further secondary structure analysis (alpha helices, beta helices and hydrogen bonding) we have been use PyMOL software (figure 2).

Figure 2 - protien structure (PyMOL)

RESULTS & DISCUSSION

The structure of p53-specific T cell receptor (PDB ID 6VTC) contains two chains which first chain consists of 3 alpha helices and 16 beta strands, second chain consists of 3 alpha helices and 20 beta strands and it also consists of hydrogen bonds present in the protein structure . There are two macromolecules

1. T-cells receptor 1a2
2. P53 specific T Cell receptor, B-chain

There are no mutations in the protein structure

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