An implementation of intelligent platform to identify new ADC targets

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Antibody drug conjugates (ADCs) are therapeutic molecules that specifically target cancer cells and offer a promising strategy in cancer treatment. As of 2022 however, only about 2% (13 cases) of ADCs have been approved by the FDA, with a limited number of target antigens (11 cases). To address this issue, our research focused on identifying new target candidates. We examined the RNA and protein expression levels for tumor-specific analysis by utilizing public databases including TCGA, GTEx, and CPTAC. This method did not reveal new targets beyond the ones already approved by the FDA. To overcome this challenge, we examined the oncogenic process of TROP2, an FDA approved target. TROP2 is cleaved by ADAM Metallopeptidase Domain 10 (ADAM10), and is associated with various cancer types, such as skin, ovary, colon, and breast cancers. We developed DS (ADC target Search), a comprehensive platform that can identify potential tumor-inducing targets cleaved by ADAM10. Structural prediction using AlphaFold2 discovers interaction motifs and features of cleavage sites between ADAM10 and various candidate targets. Karnaugh map (K-map) algorithm is utilized to generate a cut consensus sequence for various candidate targets. Machine learning is used to discover a target that meet the specified conditions. The discovered targets are categorized based on their properties (e.g. cancer types) through Enrichment Analysis. Finally, we developed and applied the DS platform algorithm which can discover new ADC targets.

Keywords: ADC, ADAM10, AlphaFold2, Cancer therapy, DS platform, TROP2