Researchers target commonly mutated or deleted gene in gynecological cancers

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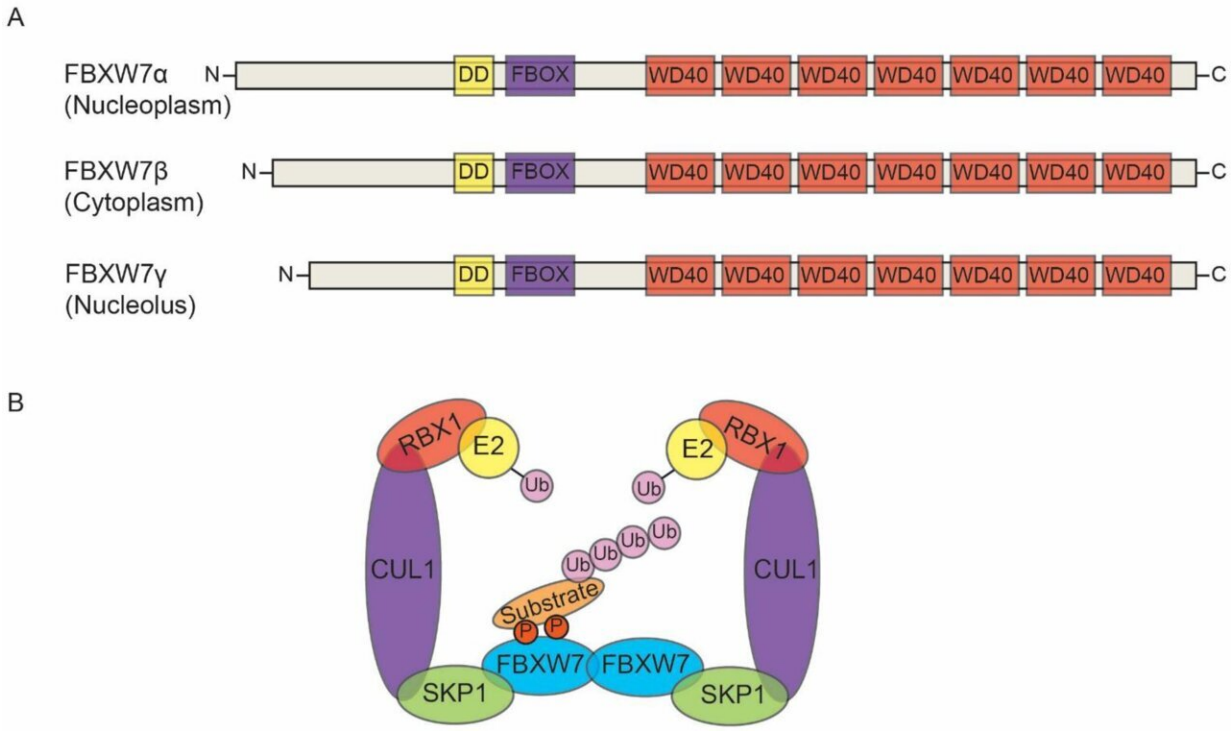

FBXW7 isoforms and SCF-FBXW7 complex. (A) Three FBXW7 isoforms (α, β, and γ), which are structurally different only at their N-terminal region, while sharing conserved domains in the C-terminal region. Each of these isoforms consists of three domains: dimerization domain (DD), F-box domain, and tandem WD40 repeats. (B) The SCF-FBXW7 complex in FBXW7 dimerization format for substrate ubiquitylation. Credit: *Cells* (2023). DOI: 10.3390/cells12101415

A gene regulating the F-Box and WD Repeat Domain Containing 7 (FBXW7) protein is frequently mutated or deleted in various types of human cancer, including gynecological cancers. Such FBXW7 mutations have been associated with poor prognosis due to increased resistance to treatment. Hence, detection of the FBXW7 mutation status may possibly serve as a suitable diagnostic and prognostic biomarker that plays a central role in determining suitable individualized management.

Antonio Giordano, M.D., Ph.D., Founder and Director of the Sbarro Health Research Organization (SHRO), has co-authored the review paper in collaboration with 9 co-authors hailing from different countries, as part of the GYNOCARE COST Action (CA18117).

GYNOCARE is a European Network for Gynecological Rare Cancer research: From Concept to Cure, which is chaired by Prof Jean Calleja-Agius, M.D., Ph.D., from the Department of Anatomy at the Faculty of Medicine and Surgery at the University of Malta, Malta. The paper by Di Fiore, R et al. is entitled "The Role of FBXW7 in Gynaecologic Malignancies" and has been published in the latest issue of *Cells*.

The FBXW7 protein has been shown to regulate cellular growth and is a well-characterized tumor suppressor. This protein is a crucial component of the Skp1-Cullin1-F-box (SCF) complex, which is a ubiquitin ligase. This complex aids in the degradation of many oncoproteins, such as cyclin E, c-JUN, c-MYC, NOTCH, and MCL1, via the ubiquitin-proteasome system (UPS).

Gynecological cancers include ovarian, uterine/endometrial, cervical, vaginal, and vulvar cancers. These malignancies pose a huge worldwide health-socio-economic burden due to their high incidence and mortality among women, irrespective of age.

Lack of screening, limited awareness of specific symptoms, late

diagnosis, or even misdiagnosis, combined with limited treatment options for advanced gynecological cancers, are the main contributing factors leading to the high morbidity and mortality, thus stressing the need for further advances in the area of gynecological cancers.

There is mounting evidence indicating that the aberrant expression of FBXW7 is involved in the development of gynecological cancers. This review provides an update on the role of FBXW7, not only as a potential biomarker, but also as a therapeutic target for novel oncologic treatments, particularly in the management of gynecological cancers.

More information: Riccardo Di Fiore et al, The Role of FBXW7 in Gynecologic Malignancies, *Cells* (2023). DOI: 10.3390/cells12101415

Provided by Sbarro Health Research Organization (SHRO)