GENETICS

BCL11A—targeting triple-negative breast cancer?

Triple-negative breast cancer (TNBC) refers to any breast cancer that does not express the oestrogen receptor (ER), progesterone receptor (PR) and HER2 receptor; this disease subtype accounts for around 15% of all breast cancer cases, and is associated with a poor prognosis. Owing to the lack of ER, PR, and HER2 expression, no targeted therapy is currently available for TNBC, leaving a combination of surgery, radiotherapy and chemotherapy as the only treatment option. Now, Walid Khaled and colleagues

have identified a gene, encoding the transcription factor BCL11A, that is overexpressed in TNBC and could provide the first rationale for a targeted treatment in this disease setting.

In this study, the investigators used a combination of genomics and experimental approaches to analyse gene expression, copy-number alterations and survival data from approximately 3,000 patients with breast cancer. “By analysing the patients’ genomics data we found that *BCL11A* is highly expressed in TNBC,” explains Khaled. He continues, “we then demonstrated experimentally that upregulation of *BCL11A* in non-tumorigenic cells drives tumour development, whereas its downregulation in TNBC cell lines leads to reduction in tumour size.” Furthermore, the researchers reported that deletion of *BCL11A* in a conditional mouse model, in either a p53-positive or p53-negative genetic background, abolishes tumour formation and maintenance. Khaled highlights, “this

is the first report showing an oncogenic role for *BCL11A* in breast cancer.”

The results of this study strongly suggest that *BCL11A* could be a good biomarker for the identification of TNBC tumours and, most importantly, that the inhibition of *BCL11A* could provide a targeted therapeutic approach for the treatment of patients with TNBC.

“In the future, we aim to assess the potential benefit of using BCL11A in breast cancer diagnosis,” says Khaled. He concludes, “the use of patient-derived xenografts will help us to further delineate the molecular function of BCL11A in TNBC pathogenesis.” In the next few years, these efforts will contribute to the development of novel drugs to target this gene and hopefully improve the prognosis of patients diagnosed with TNBC.

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Original article Khaled, W.T. *et al.* *BCL11A* is a triple-negative breast cancer gene with critical functions in stem and progenitor cells. *Nat. Comm.* doi:10.1038/ncomms6987