Researchers discover 'milk' protein that enables survival of the species

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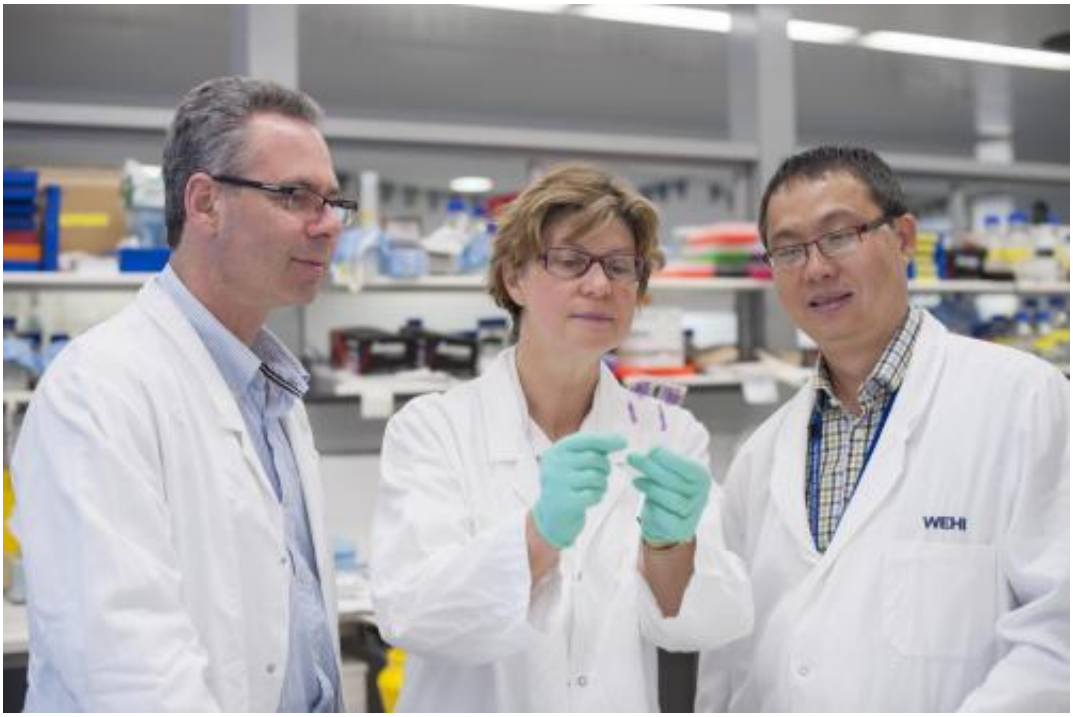

The research was led by professor Geoff Lindeman, professor Jane Visvader and Dr. Nai Yang Fu (left-right) from the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia. Credit: Walter and Eliza Hall Institute of Medical Research.

Australian researchers have discovered the protein MCL-1 is critical for keeping milk-producing cells alive and sustaining milk production in the breast. Without milk production, offspring cannot survive, making MCL-1 essential for survival of mammalian species.

Dr Nai Yang Fu, Professor Geoff Lindeman and Professor Jane Visvader from the Walter and Eliza Hall Institute led the research, published today in the journal *Nature Cell Biology*.

Professor Visvader said MCL-1 was found to be an important regulator of breast development and its milk-producing cells. "This study has unlocked one of the key survival factors in the mammary gland," Professor Visvader said.

"MCL-1 is important for all stages of breast development, from puberty to pregnancy and lactation. Based on this discovery, it is reasonable to believe that every mammal requires MCL-1 for milk production and, ultimately, the survival of their offspring."

Dr Fu said MCL-1 levels increased dramatically in the breast within 12 hours of giving birth.

"We were able to use very sensitive technologies to determine that stem cells and luminal cells were the breast cells that most critically rely on MCL-1," Dr Fu said. "Luminal cells are the cells that line breast ducts and respond to hormones during puberty, pregnancy and lactation. It now seems clear that MCL-1 is integral to the survival of these cells."

Professor Visvader said the discovery further underscored the importance of MCL-1 for cell survival. "In addition to our discovery, a number of recent research studies at our institute have shown that MCL-1 is important for the survival of certain immune cells, and for the survival and growth of cancers including leukaemia and lymphoma," she said.

"Stem cells and luminal progenitor cells both require MCL-1 for their survival. Our team has previously implicated both these cell types in some types of breast cancer, raising the question of whether MCL-1 is

an important target for developing anti-cancer drugs."

Professor Lindeman said the research also identified EGF - a growth factor - works in tandem with MCL-1 during lactation. "EGF has emerged as a key inducer of MCL-1 at the switch to lactation," he said. "It will be important to determine whether this mechanism also operates in breast cancer, as this could reveal new ways of targeting the disease."

Professor Lindeman, Professor Visvader and their breast cancer research team have spent the past 15 years unravelling the secrets of normal breast development in a bid to improve our understanding, and ultimately treatment, of breast cancer.

"You cannot fully understand how breast cancers arise without understanding normal development in the breast," Professor Visvader said. "This is an exciting time for our research team. Some of the discoveries we have made on breast development and how it goes awry in cancer have helped to identify potential targets for therapy, leading to preclinical studies and clinical trials aimed at breast cancer treatment or prevention."

More information: EGF-mediated induction of Mcl-1 at the switch to lactation is essential for alveolar cell survival, *Nature Cell Biology*, DOI: 10.1038/ncb3117

Provided by Walter and Eliza Hall Institute