

# Study finds hormones can change the breast's genetic material

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Melbourne scientists Professor Jane Visvader (left) and Dr. Bhupinder Pal (right) have discovered how female steroid hormones can make dramatic changes to the genetic material in breast cells, changes that could potentially lead to breast cancer. The researchers are from the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia. Credit: Walter and Eliza Hall Institute

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Researchers from the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, have identified how pregnancy hormones send signals to critical molecules on the DNA to make changes in the epigenome. The epigenome is a series of chemical tags that modify DNA, controlling which genes are switched on and off.

Professor Jane Visvader, Dr Bhupinder Pal, Professor Geoff Lindeman and colleagues from the institute's [breast cancer](#) laboratory led the study, which was published today in *Cell Reports*.

Professor Visvader said the researchers had created a roadmap of the [epigenomes](#) of different breast cell types. In collaboration with Professor Gordon Smyth and colleagues from the institute's Bioinformatics division they determined how the epigenomes changed in response to ovarian hormones such as progesterone.

"We found the epigenome was very sensitive to hormonal regulation," Professor Visvader said. "This reveals another way in which female hormones can influence [breast cancer risk](#) - by altering the epigenome through modifications in DNA tags."

The epigenome is where the DNA and the environment intersect, communicating signals from the outside world to the DNA. The epigenome doesn't alter the [genetic code](#), but is a layer of proteins that sits 'on top' of the DNA and provides instructions on whether DNA should be read and 'switched on' to produce proteins.

The research team found that [pregnancy hormones](#) activate a molecule called EZH2, which is an important modifier of the epigenome. "We found that hormones including progesterone activate EZH2 to modify the epigenome, leading to global changes in the expression of a huge

number of genes," Professor Visvader said.

"In normal tissue, EZH2 is essential for the development of [breast tissue](#) including ducts and milk-producing cells, and for maintaining the activity of breast stem cells and their daughter progenitor cells. However, life-long exposure to hormones could lead to breast tumour initiation through increased levels of EZH2 and the changes that it orchestrates in the epigenome."

Breast cancer is the most common cause of cancer in women, accounting for almost 30 per cent of all cancers affecting women. One in nine women in Australia will develop breast cancer by the age of 85.

High levels of EZH2 are a marker of poor prognosis in breast cancer and have been frequently observed in basal-like breast cancers, the most aggressive types of breast cancer. "The link between progesterone, EZH2 and the epigenome, could be crucially important in the very early stages of breast cancer development," Professor Visvader said.

Professor Lindeman said there were decades of evidence linking hormone exposure with breast cancer, but the hormones' influence on the epigenome was not known. "Our discovery points to a role for [hormone](#)-induced changes in the epigenome in the early stages of breast cancer initiation, and could lead to new therapeutics for treating breast cancer," Professor Lindeman said. "Inhibitors against EZH2 are being developed by others, but it will be several years before we know the outcome of these on cancer."

Provided by Walter and Eliza Hall Institute

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