Biosensors: Hormonal attractions

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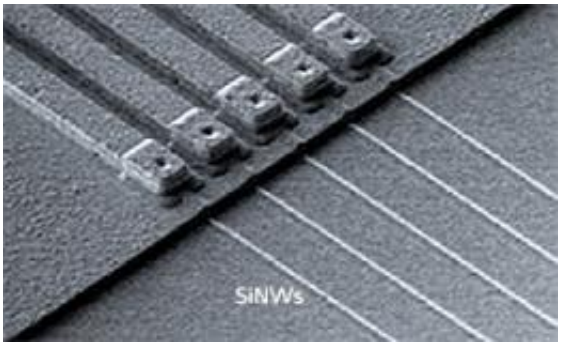

Scanning electron microscopy image of a sensor formed from five individual SiNWs. Credit: 2011 Elsevier

Estrogen receptor (ER) proteins play a major role in controlling the transcription of genetic information from DNA to messenger RNA in cells. Understanding how ER proteins interact with specific DNA regulatory sequences may shed new light on important physiological processes in the body, such as cell growth and differentiation, as well as the development and progression of breast cancer. Guo-Jun Zhang at the A*STAR Institute of Microelectronics and co-workers have now developed a detector that uses silicon nanowires (SiNWs) to evaluate these interactions.

The magnitude of the transcriptional activity that arises from the ER–DNA binding varies from one gene to another. Some genes are highly affected while others are only marginally changed. Zhang and his co-workers therefore investigated how slight variations in nucleotide

composition affect the binding affinity between ER and DNA. By combining this new information with existing experimental data on gene expression, the researchers could predict transcriptional outcome following ER–DNA binding and gain new insight into ER signaling.

Most imaging techniques developed for the study of interactions between ER proteins and DNA targets are time-consuming and require the use of fluorescent labels. A number of label-free methods exist, but they lack the sensitivity needed to distinguish subtle changes in ER–DNA binding. The new system created by Zhang's team is both label-free and highly sensitive.

The researchers prepared their ER-based sensor by modifying a nanostructured biosensing platform previously used to detect cardiac biomarkers and the dengue virus. They generated SiNW arrays on a silica substrate (pictured) through optical lithography and covered the silicon surfaces with functional organosilane and organic molecules, which allowed them to immobilize the ER proteins on the nanowires. Next, a well-shaped sample holder, constructed of insulating material, was pasted around the SiNW area.

After exposing the ER-functionalized nanowires with the target DNA, the team measured the change in resistance induced by ER–DNA complex formation to assess the binding affinity. Upon binding to ERs, DNA strands increased the overall increase in resistance of the SiNWs by adding negative charges.

The researchers discovered that the sensor could detect ultralow levels of ER-bound DNA and discriminate ER-specific from mutant DNA sequences. Moreover, the DNA easily detached from the ER-functionalized nanowires upon contact with a detergent, enabling the regeneration of the sensor.

"The SiNW array biosensor platform is now helping us in the multiplexed characterization of protein–DNA interactions," says Zhang.

More information: Zhang, G.-J. et al. Highly sensitive and reversible silicon nanowire biosensor to study nuclear hormone receptor protein and response element DNA interactions. *Biosensors and Bioelectronics* 26, 365–370 (2010). dx.doi.org/10.1016/j.bios.2010.07.129

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