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Electrochemical detection of chromosome traslocation

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Cytogenetics is a study of the cell structure with a main focus on chromosomes content and their structure. Chromosome abnormalities, such as translocations may cause various genetic disorders and heametological malignancies. Chromosome translocations are structural rearrangements of two chromosomes that results in formation of derivative chromosomes with a mixed DNA sequence. The method currently used for their detection is Fluorescent In Situ Hybridization, which requires a use of expensive, fluorescently labeled probes that target the derivative chromosomes.

We present here a double hybridization approach developed for label-free detection of the chromosome translocations. For specific translocation detection it is necessary to determine that the two DNA sequences forming a derivative chromosome are connected, which is achieved by two subsequent hybridization steps. The electrochemical impedance spectroscopy was selected as the sensing method on a microfabricated chip with array of 12 electrode sets. Two independent chips (Chip1 and Chip2) were used for targeting the chromosomal fragments involved in the translocation. Each chip was differentially functionalized with DNA probes matching the derivative chromosomes. The observed increase in the charge transfer resistance for both chips serves as a way of detection the presence of the selected translocation in the analyzed sample. The developed sensor was reliable and could in the future be implemented in cytogenetic laboratories as a supplementary method for the existing techniques.

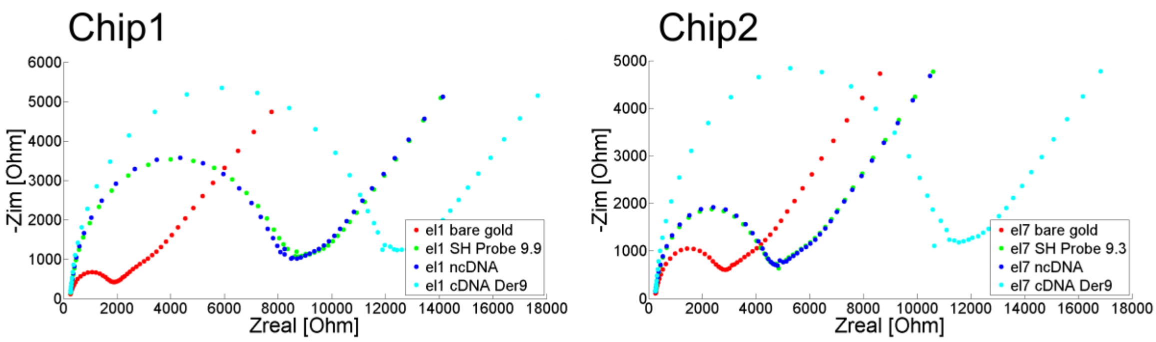

Fig.1 Chromosome Translocation Detection - Nyquist plot – EIS measurements on bare gold (red), Chip 1 SH-DNA 9.9 probe modified electrodes (green), Chip 2 SH-DNA 9.3 probe modified electrodes (green) after non-complementary DNA target hybridisation (dark blue) and after Der 9 complementary DNA hybridisation (light blue). The captured Der9 was denatured for 10 min at 95 °C and transferred manually from Chip1 to Chip2. The increase in signal on both chips indicates the translocation presence.