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Identification of inhibitors of the Fe-2OG dependent oxygenases by capillary electrophoresis with laser-induced fluorescence

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2 -oxoglutarate and Fe (II)-dependent dioxygenases catalyze the removal of N-alkyl groups from damaged DNA in eukaryotes and bacteria. Silencing these demethylating enzymes may be beneficial for the enhancement of chemotherapeutic treatments and reduction of their cytotoxic effects. Therefore, a direct and efficient quantitative analysis using biologically-relevant substrates is needed for detection of demethylase activity of *E. coli* and human Fe-2OG dioxygenases and its application for high throughput screening of potential inhibitors. Previously reported techniques utilize coupled enzyme reactions, detect coproducts, require complex processing or use radioactive substances. We developed a direct and rapid method based on capillary electrophoresis with laser-induced detection allowing real-time detection of both the substrate and the product separated with high efficiency using no post-enzymatic processing and without the use of radioactive substances. Here we report the CE-based activity assay of two members of the Fe-2OG dioxygenase superfamily of enzymes-hABH2 and hABH3, and demonstrate that the activity can be selectively inhibited by small molecules or short DNA aptamers. The inhibition selectivity of hABH2 over hABH3 enzymes can be advantageously used for qualitative and quantitative assay of these enzymes mixtures. The simple and specific differential analysis can be potentially employed to distinguish hABH2 and hABH3 enzymes expressed by the same types of cells *in vivo*. The minimal processing, short analysis time, low cost and availability of automation makes this assay useful for developing therapies targeting Fe-2OG dioxygenases.

Biography

S M Krylova has obtained her PhD from the Russian Academy of Sciences, Russia. She has over 10 years of research leadership experience in the area of Medical Diagnostics and Drug Development in biotechnology and pharmaceutical companies in Canada. She has been a contract Faculty Member at York University in Toronto since 2008. She is also leading research projects in the area of Bioanalytical Chemistry as a Senior Research Associate in the Centre for Research on Biomolecular Interactions at York University.

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