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Cytochrome 4Z1 as Selective Drug Target in Cancers: A milestone of Success

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Abstract

Background: Cytochromes P450 constitute an enzyme family involved in the oxidative metabolism of a wide variety of endogenous and exogenous compounds, including anti-cancer drugs and carcinogens. Unlike other human CYPs, CYP4Z1 is highly expressed in human breast carcinoma and is associated with poor prognosis. As a result, CYP4Z1 was hypothesised to be a potential biomarker or drug target for the discovery and development of promising anti-cancer therapies.

Objective: To screen and characterize CYP4Z1 expression as novel target for development of new anti-cancer therapies.

Method: CYP4Z1 expression was immunohistochemically screened in a set of 100 different human tissues, including normal, benign, malignant and metastatic tissues, which originated from 27 anatomical sites. Based on the above screening, CYP4Z1 expression was also evaluated in individual different tumour types. CYP4Z1 expression level for each tumour type was correlated with histopathological features, prognostic immunohistochemical markers and patient survival.

Results: CYP4Z1 was expressed in only one (4.3%) of the normal tissues from the mammary glands, while the expression of the enzyme was positive in 1 (11%), 12 (19%) and 2 (40%) of the benign, malignant and metastatic tissues, respectively. Interestingly, several tumour entities showed prominent expressions of CYP4Z1, including carcinomas of adrenal cortex, squamous cells of oesophagus, lung and cervix, as well as seminoma, astrocytoma, melanoma and lastly endometrial adenocarcinoma. For individau tumour types, CYP4Z1 was highly expressed in cancers of berast, bladder, colon, cervix,ovary and lung. Importently, CYP4Z1 expression was identified an independent prognostic predictor of poor survival in cancer patients.

Conclusion: CYP4Z1 was distinctly overexpressed in benign, primary and metastatic cancer tissues compared to corresponding normal tissues. This differential in CYP4Z1 expression across different types of cancers strongly supports CYP4Z1 as potential biomarker and target for novel anticancer therapy development.

Keywords: cancer, cytochrome P450, cytochrome 4Z1, immunohistochemistry.

Biography

Dr. Al-saraireh is an associate professor of cancer pharmacology at Mutah University – faculty of medicine. He has finished both his Msc and PhD degrees from Bradford University - UK. Dr. Al-saraireh is interested in the studies of orphan cytochromes, glypicans and glycans and their relation to cancer development and progression. He is also interested in the development of new techniques evaluating tumour immigration and metastasis. After graduation, Dr. Alsaraireh has published 40 research papers, over 30 of which were in the field of cancer pharmacology and the vast majority of them were in tumour enzymology. He is also a teaching faculty for the first, second and third year MD students and he is responsible for teaching them both general pharmacology and system specific pharmacology.

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