NEW APPROACH TO CANCER THERAPY: HIF2α INHIBITORS

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Abstract

Hypoxia is a common feature associated with many types of cancer. Insufficient oxygenation state intensifies genome instability, promotes progression, enables avoidance of the immune response, and takes part in developing more aggressive phenotypes resistant to chemotherapy, radiotherapy, and photodynamic therapy. The activity of the hypoxia-inducible factor, the critical element of response and adaptation to hypoxia, enhances cancer hallmarks such as suppression of the immune response, altered metabolism, angiogenesis, invasion and metastasis, and more. Although the HIF transcriptional factor is an intensively researched target of antitumor therapy, currently used agents target it indirectly (through topoisomerase I, mTOR, HSP90, etc.). The new inhibitors, PT2385, and PT2977 are first-in-class compounds targeting HIF directly. Moreover, they target isoform HIF2α, which is believed to maintain chronic hypoxia that characterizes advanced tumors. This poster briefly summarizes basic knowledge about hypoxia in cancers and activity of the hypoxia-inducible factor, shows structures of the new agents and discrepancies between their activity and previously used inhibitors. The poster also includes the preliminary results of PT2385 clinical trials and the schedule of the next planned clinical trials. This poster aims to signal the appearance of the new approach in the field of inhibiting the hypoxia-inducible factor.

Recent Publications

Kozal K. **Role of the hypoxia-inducible factor in the metabolism of cancers and its inhibitors in anticancer therapy**., Nauka, Badania i Doniesienia Naukowe 2020: Nauki przyrodnicze i medyczne / Wysoczański Tobiasz (eds.), vol. 1, 2020, Idea Knowledge Future, ISBN 978-83-953882-6-2, pp. 79-87

Jóźwiak, P., Ciesielski, P., Forma, E., **Kozal, K.**, Wójcik-Krowiranda, K., Cwonda, Ł., Bieńkiewicz, A., Bryś, M., & Krześlak, A. (2020). **Expression of voltage-dependent anion channels in endometrial cancer and its potential prognostic significance**. Tumor Biology. https://doi.org/10.1177/1010428320951057

Jóźwiak P, Ciesielski P, Zakrzewski PK, **Kozal K**, Oracz J, Budryn G, Żyżelewicz D, Flament S, Vercoutter-Edouart A-S, Bray F, Lefebvre T, Krześlak A. **Mitochondrial O-GlcNAc Transferase Interacts with and Modifies Many Proteins and Its Up-Regulation Affects Mitochondrial Function and Cellular Energy Homeostasis.** Cancers. 2021; 13(12):2956. https://doi.org/10.3390/cancers13122956



Biography

Karolina Kozal is a student of second-degree biology studies with a specialization in biochemistry and molecular biology at the University of Łódź, Poland. She holds a Bachelor of Science degree in Medical Biology with a specialization in biochemical and molecular diagnostics obtained at the University of Gdańsk, Poland. Karolina Kozal is involved in research projects in the Department of Cytobiochemistry in the Institute of Biochemistry at the University of Lodz, Poland.

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