

Posters

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SELECTIVE INHIBITION OF CARBONIC ANHYDRASE IX FOR CANCER DIAGNOSIS AND THERAPY

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Carbonic anhydrase IX (CA IX) belongs to a group of 15 isoforms of the human carbonic anhydrase enzymes. Typically localized on the cell surface, CA IX is primarily found in specific tissues within the gastrointestinal tract. Its expression is induced in response to local hypoxia, aiding in the regulation of pH levels to accommodate the metabolic production of acidic by-products, thereby promoting cancer cell survival and proliferation. The overexpression of CA IX in solid tumors, coupled with its extracellular presence, suggests its potential utility in cancer diagnosis and therapy.

Primarily, most of CA IX inhibitors feature sulphur-based functional group that coordinates the Zn²⁺ ion in the active site. Although overexpression of CA IX is predominantly associated with tumor tissues, other isoforms are present in normal tissues that contributing critical physiological processes. The high sequence similarity and structural homology among CA isoform family causes off-target inhibition leading to unintended side effects. This underscores the need for developing highly selective inhibitors that minimize off-target effects. The project aims to address these challenges by designing novel functional group to enhance both the affinity and selectivity of CA IX inhibitors.

The active site of CA is situated within the central -sheet, where the zinc-binding core serves as a key junction for the proposes inhibitors, which are designed with a

scaffold capable of attaching enzyme moieties. This scaffold comprises a sulfonimine binding group for metal ion interaction, a functional group for interaction with the hydrophobic regions, and additional heteroaromatic moieties to improve affinity. Structural optimisation of these inhibitors has been conducted by understanding how they are fitting within the enzyme's active site, in order enhancing their affinity for tumor-specific CA IX while restricting interactions with other CA isoforms. Additionally, some potent chelators have been selected for theranostics applications, ensuring they do not compromise the binding capacity of inhibitors.

Recombinant CA IX is produced and expressed in *Escherichia coli* BL21, followed by purification via several chromatographic steps to ensure high protein purity. The purified CA and a series of inhibitors are assessed for affinity using the stopped-flow method to screen a library of inhibitors. To better understand the binding modes between selective inhibitors and the enzyme, X-ray crystallography is employed to achieve high-resolution structures of the compounds. The obtained structural information will guide the modification and optimisation the anchored and sticky groups in design the selective inhibitors. This approach aims to maximize affinity for tumor-specific CA IX while minimizing interactions with other carbonic anhydrase isoforms.



SCHOOL GARDENS - AN ENVIRONMENT FOR RESEARCH AND TEACHING BIOSCIENCE

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School gardens are among the most frequently used spaces for outdoor education, as they provide ample space for experimentation in proximity to educational institutions [1]. By teaching in garden areas, we are continuing the principles of Jan Amos Komenský and the tradition of outdoor teaching from the time of Maria Theresa [2]. When teaching in nature, students' knowledge is linked to practical use, pro-environmental attitudes are formed, creativity is

developed, and cooperation, perseverance, and responsibility are trained [3].

School gardens are also an essential place for learning about plant ecosystem services. Biology teachers and students can use modern measuring technology, such as thermal imaging cameras, IR thermometers, CO₂ meters, etc., during garden-based experiments to learn about the physiological processes through which plants influence the hu-



man environment and contribute significantly to mitigating the effects of global climate change. Field teaching activities are part of STEM education. Through their knowledge of plant teachers and their students become aware of the importance of plants. Teaching in school gardens is thus becoming a recognized way of combating the phenomenon of "plant blindness," [4].

In the school's garden, we can also observe non-living nature. An ideal topic for exploring the complex connections between life and earth sciences is the evolution of land use and land cover. Shifts in vegetation, land cover, and land use—driven by variations in climate, bedrock composition, and, above all, human activity—are often clearly visible also in the vicinity of schools. Teaching in garden areas (with using of appropriate methods and tools, e. g. maps or aerial photographs) is a way of incorporating the described topic into regular lessons and to provide the integrated teaching also in the outdoor environment.

Gardens at schools and other academic institutions also play an essential role in education, as they serve as valuable sites for research activities conducted by scientists and students. Such gardens provide a space where research questions can be explored in the context of student projects and diploma thesis and dissertation. Moreover, they often encompass a broad range of biotopes and habitats, thereby offering opportunities to address a wide spectrum of zoological and ecological research topics (e.g., 1) small water reservoirs embedded in the soil serve as mesocosms for the study of aquatic communities[5][6]; 2) a source of organisms for research into insect dispersal abilities[7][8](; 3) a research site for studying cold tolerance and microhabitats of overwintering of insects[9][10].

Other type of research is currently underway focusing on determining bioactive substances in cultivated crops, particularly in various varieties of common vegetables and selected medicinal plants. The bioactive substances being determined mainly include the content of total phenolic compounds, vitamin C, chlorophylls, and carotenoids in plant parts intended for consumption. Edible are grown in the garden, and the dominant flavonoids - quercetin, kaempferol, and myricetin - are also determined [11]. The research also focuses on the cultivation of non-traditional vegetables and their benefits for human health.

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