Challenge Project Initial Bibliography: 17GS

[1] Bocedi A, Noce A, Marrone G, Noce G, Cattani G, Gambardella G, Di Lauro M, Di Daniele N, Ricci G. Glutathione Transferase P1-1 an Enzyme Useful in Biomedicine and as Biomarker in Clinical Practice and in Environmental Pollution. Nutrients. 2019 Jul 27;11(8):1741. doi: 10.3390/nu11081741. PMID: 31357662; PMCID: PMC6723968.

Annotation:

This article states the pivotal role of Glutathione Transferase P1-1 (GSTP1-1), an enzyme abundant in mammalian erythrocytes, in detoxifying cells from toxic compounds through glutathione utilization or acting as a ligandin. GSTP1-1's potential as a biomarker in various fields is underscored, with particular emphasis on its application in detecting blood toxicity in patients with kidney diseases. The enzyme's overexpression in erythrocytes under toxic conditions suggests its utility in monitoring chronic kidney disease, assessing dialysis adequacy, and evaluating the efficiency of kidney transplants. Furthermore, GSTP1-1's elevation in autoimmune diseases like scleroderma indicates its broader relevance in pathological conditions. The review also explores GSTP1-1's involvement in oxidative stress and its implications in cancer, liver and neurodegenerative diseases, psychiatric disorders, and its promising use in environmental health, monitoring individuals in polluted areas, and in veterinary science.

This article focuses on the development of biosensors for blood toxicity and the assessment of dialysis adequacy in kidney disease patients. It could also contribute to discussions on the role of biomarkers in the management of autoimmune diseases, organ transplantation, and the broader implications of GSTP1-1 in oxidative stress, environmental health, and various human pathologies.

[2] Widersten M, Kolm RH, Björnestedt R, Mannervik B. Contribution of five amino acid residues in the glutathione-binding site to the function of human glutathione transferase P1-1. Biochem J. 1992 Jul 15;285 (Pt 2)(Pt 2):377-81. doi: 10.1042/bj2850377. Erratum in: Biochem J 1992 Nov 1;287(Pt 3):1023. PMID: 1637329; PMCID: PMC1132797.

Annotation:

This study explores the effects of site-specific mutagenesis on the catalytic activity and substrate specificity of human Class Pi glutathione transferase (GST) P1-1, an enzyme crucial for detoxifying cells. Five amino acids within the active-site cavity, proximal to the bound glutathione (GSH), were targeted for mutation: Arg14 to Ala, Lys45 to Ala, Gln52 to Ala, Gln65 to His, and Asp99 to Asn, with Gln65 to Ala also attempted but not characterized due to poor catalytic activity. The mutations resulted in dimeric proteins that retained catalytic activity but exhibited a roughly 10-fold decrease in GSH affinity, indicating these residues' importance in GSH binding. The Arg14 mutation also significantly reduced enzyme stability, highlighting its structural role. The Asp99 mutation affected the enzyme's catalytic mechanism, suggesting Asp99's involvement in proton transfer. Lys45 to Ala mutation altered the enzyme's substrate specificity, demonstrating an increased catalytic efficiency with GSH monoethyl ester over natural GSH.

[3] Ricci G, Caccuri AM, Lo Bello M, Parker MW, Nuccetelli M, Turella P, Stella L, Di Iorio EE, Federici G. Glutathione transferase P1-1: self-preservation of an anti-cancer enzyme. Biochem J. 2003 Nov 15;376(Pt 1):71-6. doi: 10.1042/BJ20030860. PMID: 12877654; PMCID: PMC1223740.

Annotation:

This passage introduces the concept of 'co-operative self-preservation' in the enzyme human glutathione transferase P1-1, a mechanism that allows the enzyme to protect itself against threats such as competitive and irreversible inhibitors, high temperatures, and UV radiation. This self-preservation is achieved through structural intersubunit communication, where one subunit can trigger a defensive response in another subunit in response to inactivating modifications. This mechanism is highlighted as an evolutionary adaptation aimed at enhancing cellular survival by maintaining the enzyme's detoxifying and anti-cancer activities.

The big ideas discussed here involve the intricate self-defense mechanisms at the molecular level in enzymes, evolutionary biology, and the implications of such mechanisms for cancer treatment. The discovery of this self-preservation strategy in an enzyme typically overexpressed in tumor cells illuminates the challenges faced in developing effective chemotherapy treatments, as this mechanism can interfere with pharmacological efforts to inhibit the enzyme and combat drug resistance. This source could inform the section on molecular biology or biochemistry, focusing on enzyme structure and function.

[4] Pereira SAP, Baptista L AC, Biancalana L, Marchetti F, Dyson PJ, Saraiva MLMFS. Automated approach for the evaluation of glutathione-S-transferase P1-1 inhibition by organometallic anticancer compounds. J Enzyme Inhib Med Chem. 2022 Dec;37(1):1527-1536. doi: 10.1080/14756366.2022.2073443. PMID: 35635138; PMCID: PMC9176637.

Annotation:

This passage describes an innovative automated method utilizing Sequential Injection Analysis to measure the activity of GST P1-1. The method focuses on evaluating the enzyme's activity in the presence of organometallic complexes that have potential anticancer properties, by monitoring the formation of a product through changes in absorbance. The assay's efficiency is demonstrated through its application to various metal complexes, identifying an iridium compound as a particularly potent inhibitor of GST P1-1.

The big ideas revolve around the integration of analytical chemistry techniques with cancer research, particularly in the search for effective inhibitors of enzymes associated with drug resistance. This source could inform sections of a project focused on analytical chemistry, especially those detailing the development and optimization of assays for biochemical analysis.