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September 03-04, 2018 | Bangkok, Thailand

ACCEPTED ABSTRACTS

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FACTORS INFLUENCING ATTRITION AMONG PATIENTS RECEIVING ANTI-RETROVIRAL THERAPY IN THE ACCRA REGIONAL HOSPITAL

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Introduction: Human immunodeficiency virus and acquired deficiency syndrome (HIV/AIDS) epidemic remains a global health challenge. Addressing the issue of attrition is critical for ending the epidemic. We therefore sought to determine the factors influencing attrition among patients receiving antiretroviral therapy in Accra Regional Hospital (Ridge Hospital).

Methods: Retrospective study design was adopted using routinely collected data of National AIDS Control Programme (NACP) on HIV/AIDS patients receiving care from 2006 to 2017 at Greater Accra Regional Hospital. Convenience sampling is used to select the study area and unit. All gathered data was exported to STATA statistical software package for analysis including descriptive, trend and survival analysis.

Results: Between January 2006 and December 2017, 4,330 people living with HIV were enrolled into care. Of them, 196 (4.53%) died and 1,166 (26.93%) were loss to follow-up (LTFU). Enrollment peaked with increased campaigns in 2008 and then fell with expansion of treatment sites in Greater Accra region. LTFU mimicked changing enrollment; deaths peaked with shortage of ARVs in 2015. The determinants of LTFU were: Muslims (aHR: 1.296; CI: 1.034-1.625); CD4 count <250 (aHR: 1.546; CI: 1.308-1.828); other funding source (aHR: 0.736; CI: 0.579-0.935); completed counselling (aHR: 1.328; CI: 1.093-1.613); disclosed status (aHR: 0.798; CI: 0651-0.978). Predictors of mortality were: more than 54 years of age (aHR: 2.915; CI: 1.165-7.297); male gender (aHR: 1.507: CI: 1.051-2.160); being divorced/separated (aHR: 1.763; CI: 1.014-3.064); CD4 count <250 (aHR: 1.069; CI: 1.027-2.797); funded by special project (aHR: 0.393: CI: 0.185-0.835).

Conclusion: The trend of attrition was influenced by institutional and national events. Factors influencing attrition in the hospital is comparable to those found in other parts of Africa and Asia. Interventions should therefore be implemented for optimal health.

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DECODING THE AMINO ACID SEQUENCE OF A PROTEIN TO EXTRACT ITS FOLDING INFORMATION

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The problem how a unique and complex protein 3D structure forms is a long-standing problem in structural biology. It is very interesting how the folding information of a protein can be extracted from its sequence. When we make a plot of a pair of residues with the shorter average distance on a contact map so that the average distance of a residue pair <r> shows a scaling rule N1/3 in an implicit way, a region to be compact can be predicted along the amino acid sequence of a protein. Furthermore, an effective inter-residue potential can be defined based on the inter-residue average distance statistics. The contact frequency of a residue with other residues will provide information of a site of the initial folding events of a protein. We call the contact frequency F value. Thus, we consider that conserved hydrophobic residues during the evolution around a peak of the contact frequency plot of a protein have a significant role on the folding of a protein. In this study, the effectiveness of the present method is examined taking proteins with characteristic 3D structures such as lysozyme related proteins, β-trefoil proteins and so on. The results are compared with those of HD-exchange or Φ-value experiments. A, F, L, M, V, Y, W are taken as hydrophobic residues in this study. Furthermore, evolutionary analysis is also conducted with the phylogenetic tree of proteins in a superfamily. The common mechanisms of the proteins in a superfamily are discussed. We also discuss the general mechanism of protein folding.

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BIOCHEMICAL & BIOPHYSICAL CHARACTERIZATION AND THERMODYNAMIC COMPARISON OF DIFFERENT VARIANTS OF THE REDOX SELENOZYME THIOREDOXIN GLUTATHIONE REDUCTASE OF *FASCIOLA GIGANTICA*

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The thiol-disulfide redox metabolism in platyhelminth parasites depends entirely on a single selenocysteine (Sec) containing flavoenzyme, thioredoxin glutathione reductase (TGR) that links the classical thioredoxin (Trx) and glutathione (GSH) systems. In the present study, we investigated the catalytic and structural properties of different variants of *Fasciola gigantica* TGR to understand the role of Sec. The recombinant full-length Sec containing TGR (FgTGRsec), TGR without Sec (FgTGR) and TGRsec without the N-terminal glutaredoxin (Grx) domain (ΔNTD-FgTGRsec) were purified to homogeneity. Biochemical studies revealed that Sec597 is responsible for higher thioredoxin reductase (TrxR) and glutathione reductase (GR) activity of FgTGRsec. The N-terminal Grx domain was found to positively regulate the DTNB-based TrxR activity of FgTGRsec. The FgTGRsec was highly sensitive to inhibition by auranofin (AF). The structure of FgTGR was modeled, the inhibitor AF was docked, and binding sites were identified. Unfolding studies suggest that all three proteins are highly cooperative molecules since during GdnHCl-induced denaturation, a monophasic unfolding of the proteins without stabilization of any intermediate is observed. The Cm for GdnHCl induced unfolding of FgTGR was higher than FgTGRsec and ΔNTD-FgTGRsec suggesting that FgTGR without Sec was more stable in solution than the other protein variants. The free energy of stabilization for the proteins was also determined. To our knowledge, this is also the first report on unfolding and stability analysis of any TGR.

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STRUCTURAL BASIS FOR LIPID-DEPENDENT GATING OF A KV CHANNEL

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Lipid-dependent gating refers to our observations that lipid molecules without phosphate groups in their headgroup regions, called nonphospholipids, favor the resting state of the voltage-sensor domain in a voltage-gated potassium (Kv) channel whereas phospholipid molecules favor the activated state. More studies suggest that the annular lipids and a Kv channel form a functional unit and both nonspecific and specific interactions at the protein-lipid interface contribute to the energetic differences of the channel in different gating states. Since our discovery of the phenomenon in KvAP, similar results have been obtained from other voltage-gated ion channels in both *in vitro* and *ex vivo* systems, suggesting that the lipid-dependent gating could be a more generic gating mode for other voltage-gated ion channels. To analyze the conformational changes of a Kv channel in different lipids, we obtained a peptide-binder that recognizes a non-phospholipid-stabilized resting state of the KvAP voltage sensor and found that attachment of the peptide to the C-terminus of the channel appears to keep it in the resting state in phospholipid membranes. We analyzed the structure of the KvAP-peptide fusion protein by single particle cryoEM and revealed a voltage-sensor ring that may keep the voltage-sensor paddle in a resting state where all its arginine residues face the intracellular side of the gating pore with the tip of the S3S4 paddle leaning against the splayed-open S1/S2. The structural features of the new model are different from the four-helix bundle structure of the voltage sensor domain in the activated conformation and allow the S3/S4 to face annular lipids directly. Such structural arrangements could explain a set of biochemical data we obtained from different channel mutants and reveal new insights on the possible movement of the voltage sensor domain to achieve its gating control of the ion-conducting pore. Another surprise from the cryoEM study is that an unknown protein binds tightly to the extracellular side of the KvAP pore domain. MS spectrometry and proteomic analysis suggested a few candidates that need further characterization. We are investigating whether the new pore-binders play a role in the lipid or voltage-dependent gating of the channel.

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UTILIZING THE PHYSICAL, CHEMICAL AND STRUCTURAL PROPERTIES OF SYNTHETIC BIO-RECEPTORS (APTAMERS) FOR THE DEVELOPMENT OF BIO-SENSORS FOR DIAGNOSTIC APPLICATIONS

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Double stranded DNA plays a crucial role in information transfer and evolution. However, in single stranded form, the DNA molecule is unstable and prefers to stabilize itself by associating with available reactive groups. In 1990, Szostak and Gold labs independently developed techniques that enables *in vitro* evolution of nucleic acids capable of binding targeted compounds with high affinity and specificity. The process of generating these functional nucleic acid species (also known as aptamers) was termed systematic evolution of ligands by exponential enrichment (SELEX). Aptamers have been generated to target a plethora of molecules ranging from ions to whole cells. However, developing single stranded DNA aptamers capable of binding to small molecular targets pose some complexities. This talk will elaborate on the intricacies of developing highly selective ssDNA aptamers capable of binding a plethora of organic small molecules such as estradiol, bisphenol A, triclosan, and glyphosate for use in a variety of biological and environmental matrices. Once the target binding characteristics of the identified aptamers is determined, the aptamers unique physical, chemical and structural properties is utilized to develop a variety of sensing platforms such as Eastern blotting, dynamic light scattering-resistive pulse sensing, gold nanoparticle-based sensing, impedance spectroscopy, lateral flow, enzyme linked oligonucleotide assay (ELONA) and microfluidic applications. The developed assay formats reached detection limits as low as femtomolar levels demonstrating the important role aptamers will play in future diagnostic applications.