Interference of Zinc Chelation with Cancer Cell Proliferation

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Cell division is a complex process tightly regulated by several classes of genes. Cancers occur primarily due to misregulation of this machinery, resulting in uncontrolled growth of cells. We recently showed that the transition metal chelator, TPEN, blocks entry into meiosis of Xenopus oocytes and targets a protein involved in cell cycle: Cdc25c. Cdc25c is a dual specificity phosphatase that plays crucial roles in cell cycle progression particularly during the G2-M transition of the cell cycle. Analysis of recombinant Cdc25c metal content revealed that Cdc25c is a Zn$^{2+}$-binding metalloprotein (Lu Sun et al., 2005).

Based on these findings we hypothesize that Zn$^{2+}$ is an important cofactor for Cdc25c to adopt the right conformation to recognize and interact with its substrate Cdc2. To test this hypothesis, we used Arabidopsis Cdc25c because the Zn-coordinating residues have been identified in this protein. This analysis identified the following residues as potential Zn-coordinating residues: H420, C507, C513, H516, and H517. To test whether these residues coordinate Zn we have mutated them to Ala and are presently purifying the mutant and wild-type proteins as recombinant proteins to test their phosphatase activity and ability to induce entry into M-phase following microinjection into oocytes.

Patterns of HIV Infection Among Spousal and Cohabiting Sexual Partnerships in Sub-Saharan Africa

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Background: The reasons behind the differences in the levels of discordancy (that is one partner testing HIV positive while the other testing HIV negative) among spousal and cohabiting partnerships affected by HIV across sub-Saharan Africa (SSA) remain inadequately understood. Recently, many randomized clinical trials have shown substantial efficacies for several prevention interventions among these partnerships.

Moreover, there has been an intense debate about the priority of HIV prevention interventions among discordant couples relative to other prevention approaches such as among commercial sex networks.

Objective: To describe and explain patterns of HIV infection among spousal and cohabiting sexual partnerships, across a range of settings in SSA.

Methods: Demographic health survey (DHS) data for 20 countries in SSA were used to estimate the prevalence of HIV sero-discordancy among stable partnerships with at least one HIV-infected individual in the partnership (P), prevalence of discordancy among all stable partnerships in the population (S), prevalence of discordancy among the entire sexually active population (A), and prevalence of discordancy among HIV infected individuals (I).

Results: Two distinct patterns of HIV among stable partnerships were observed. Countries with low HIV prevalence had a high discordancy prevalence among P and I ranging from 48.4-87.8% and 30.6-60.0%, respectively, but low discordancy prevalence among S and A ranging from 0.4-6.4% and 0.2-3.8%, respectively. Conversely, countries at hyper-endemic HIV epidemics had a low discordancy prevalence among P and I ranging from 36.3-58.5% and 17.2-46.0%, respectively, but high discordancy prevalence among S and A ranging from 9.3-17.2% and 5.8-8.3%, respectively.

Conclusions: Two distinct patterns of HIV in stable partnerships were observed. In high prevalence settings, many partnerships were affected by HIV but relatively few were discordant, whilst the opposite was true for low prevalence settings. This pattern may be arising from variations in the HIV transmission probability which is dependent on biological and behavioral factors and might also be affected by the frequency of infection from external partners especially in high prevalence countries. These findings may complicate considerations for rolling out prevention interventions among stable discordant partnerships in SSA.