

P021 A role for PrP^C in neuronal zinc metabolism

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Whilst an exact physiological function remains elusive for the cellular isoform of the prion protein (PrP^C), an involvement in metal homeostasis has been proposed. To date, this work has centered on copper metabolism, evaluating roles on binding and uptake of the ion. However, there is a possible role for PrP^C in neuronal zinc (Zn) homeostasis. Zn has been shown to bind at the octapeptide repeat sequence and induce endocytosis of the protein. Furthermore, an increase in Zn-bound PrP^C was determined in affinity purified material from prion-infected mice. In order to evaluate whether PrP^C is involved in neuronal Zn uptake, two Zn-sensitive fluorochromes were used. Zinpyr-1 staining indicated that cells exposed to increasing Zn concentrations in their media showed significant time- and dose- dependent increases in Zn-associated fluorescence; an effect which was enhanced in cells expressing PrP^C. Newport Green measurements determined that the rate of Zn uptake was also enhanced in the presence of PrP^C. Knockdown of endogenous PrP gene expression by siRNA reduced Zn uptake. Significantly, when the endocytosis of PrP^C was inhibited, Zn uptake could still be measured suggesting that an alternative mechanism was responsible for the increases in intracellular Zn. Further studies to determine this mechanism are being investigated. These data demonstrate a role for PrP^C in the cellular uptake of Zn ions potentially demonstrating a novel physiological function for the protein.