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Manganese and Parkinson's Disease: new findings through a yeast protein study

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Parkinson Disease (PD) is a neurodegenerative pathology whose causes have not been yet fully clarified. For this reason it is also called an idiopathic (with no known or identifiable causes) syndrome, although some PD types can have a genetic or a post-traumatic origin, and different risk factors like exposure to some pesticides. Recently it emerged that also exposure to manganese (i.e. in welders or miners) can cause a PD-like syndrome (Parkinsonism), and a connection between genetic and environmental causes of Parkinson's disease has been discovered: a genetic interaction between two Parkinson's disease genes (alpha-synuclein and PARK9, alias ATP13A2) was found, and it was determined that the PARK9 protein can protect cells from manganese poisoning [1].

Shortly after, a study on a yeast gene, YPK9, which is 58% similar and 38% identical in its amino acid sequence to human PARK9, revealed that deletion of this gene confers sensitivity for growth for cadmium, manganese, nickel and selenium, suggesting that the YPK9 protein may play a role in the sequestration of divalent heavy metal ions [2]. In the same way, a mutation on PARK9 may expose humans to these cations, especially to manganese.

In this perspective, we have chosen short fragments of YPK9 protein that included interesting sequences for metal binding and studied their behaviour towards divalent cations such as manganese and calcium, using NMR mono- and bidimensional techniques and EPR spectroscopy. If metal binding were clearly assessed in the yeast analogue, we could get a hint of what may happen in humans. Here we would like to present our latest findings.

References:

[1] Gitler, A.D.; Chesi, A.; Geddie, M.L.; Strathearn, K.E.; Hamamichi, S.; Hill, K.J.; Caldwell, K.A.; Caldwell, G.A.; Cooper, A.A.; Rochet, J.-C.; Lindquist, S., *Nat. Genet.* **2009**, Vol. 41, pp 308-315.

[2] Schmidt, K.; Wolfe, D.M.; Stiller, B.; Pearce, D.A., *Biochem. Biophys. Res. Comm.* **2009**, Vol. 383, pp. 198-202.

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