

P006 ZIP7 controls intracellular zinc distribution providing a breast cancer target

KM Taylor, N Jordan, S Hiscox and RI Nicholson

Welsh School of Pharmacy, Cardiff University, Redwood Building, King Edward VIIth Avenue, Cardiff, CF10 3XF, UK.

There is paucity of mechanistic information concerning control of cellular zinc homeostasis by zinc transporters. We have used our model of zinc-dependant signalling to demonstrate a key role for zinc transporter ZIP7 in intracellular zinc distribution.

We have observed elevated intracellular zinc in our model of Tamoxifen-resistant breast cancer which utilises EGFR, IGF1-R and Src signalling to drive the increased growth/invasion and increased expression of ZIP7 (SLC39A7/HKE4), a molecule established by us capable of increasing intracellular zinc.

We demonstrate a zinc-dependant activation of these signalling pathways, as well as additional increases in cell growth and invasion. Moreover we show a major role for ZIP7 in the zinc-induced activation of EGFR, Src, and IGF1-R which was eradicated in the presence of ZIP7 siRNA. Furthermore, we observed increased activation of signalling and invasion by transfecting recombinant ZIP7 into wild-type cells.

These results combine to reveal a key role for ZIP7 in intracellular zinc distribution, agreeing with recently published data, and pinpointing ZIP7 as a candidate for the execution of the intracellular zinc wave, thought responsible for phosphatase inhibition, and thus providing ZIP7 as a new target for tyrosine kinase inhibition in diseases such as breast cancer.