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NEUROENDOCRINE CANCER

Insulinomas—recurrent mutations identified in YY1

A paper published in *Nature Communications* reports the identification of new mutations in insulinomas, the most common type of functional pancreatic neuroendocrine tumours.

"Aside from loss-of-function germline mutations in *MEN1*, no other common genetic cause had been identified in functional pancreatic neuroendocrine tumours," explains corresponding author Guang Ning. The researchers, therefore, performed whole-exome sequencing of 10 sporadic insulinomas. This analysis identified novel recurrent mutations in the *YY1* gene (which encodes the transcriptional repressor YY1). All the mutations result in a Thr372Arg change.

To validate these findings, the researchers used Sanger sequencing and pyrosequencing to screen a further 103 insulinomas. The Thr372Arg mutation was found in 30% of the tumours; "to find a recurrent mutation in the exact same amino acid in 30% of samples is highly unusual," notes Ning. The cohort was then divided into two groups—those with the Thr372Arg mutation and those without the mutation (wild-type) to assess the clinical importance of the mutation. Patients with the Thr372Arg mutation had a later onset of tumours than did patients with wild-type *YY1* (mean age of 56 years versus 46 years).

"Identifying an oncogene that has an important role in the development of insulinomas is of great significance, as it might help identify novel targets for therapeutic intervention for this highly detrimental disease," explains Ning. The research team is now planning to explore the importance of the YY1 protein in pancreatic β cells both *in vitro* and *in vivo*.

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Original article Cao, Y. *et al.* Whole exome sequencing of insulinoma reveals recurrent T372R mutations in *YY1*. *Nat. Commun.* doi:10.1038/ncomms3810