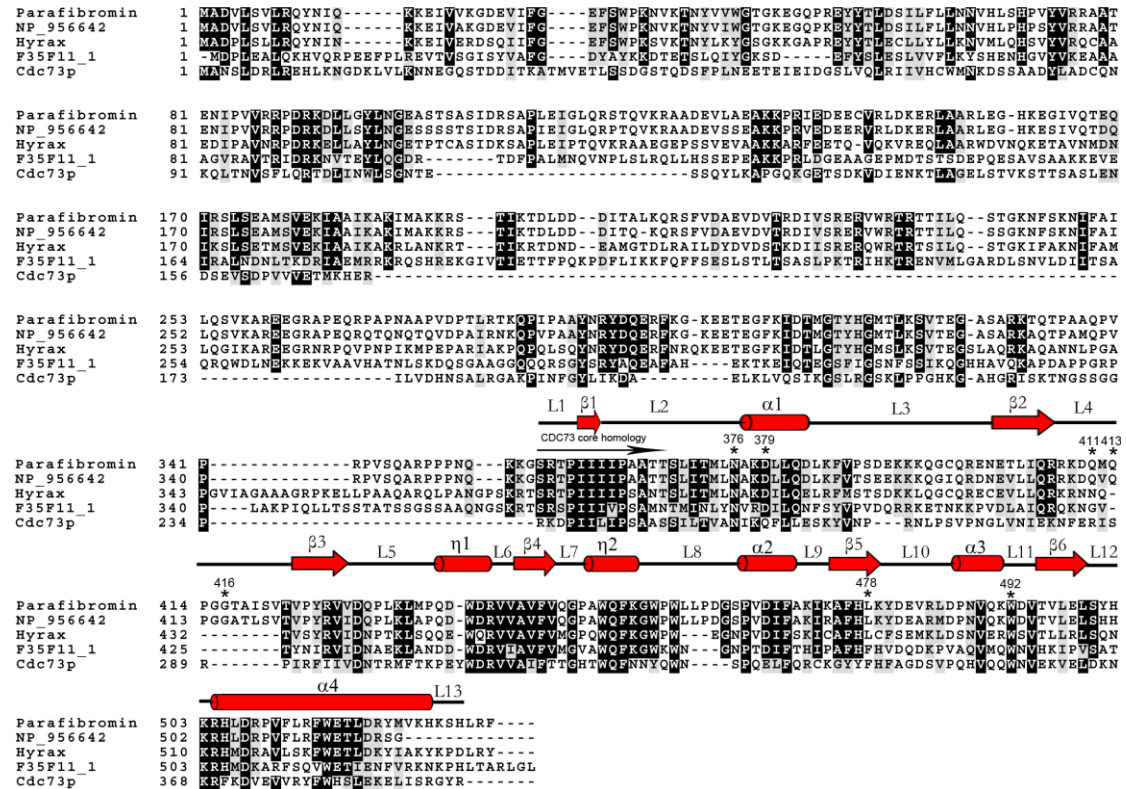


Supplementary Material

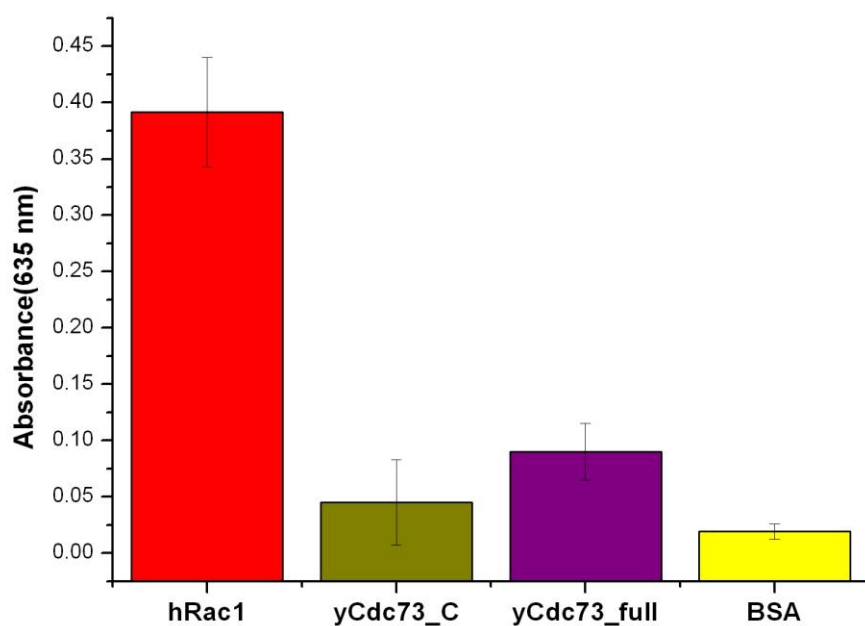


Supplementary Figure 1

Sequence alignment between yCdc73 and other homologous proteins from metazoan species. Cdc73 (*Saccharomyces cerevisiae*) homologs shown are Parafibromin (*Homo sapiens*) NP 956642 (*Danio rerio*), Hyrax (*Drosophila melanogaster*) and F35F11.1 (*Caenorhabditis elegans*). The star symbols indicate these mutations in the C-terminal domain of hCdc73.

Supplementary Fig.2

Bar graph diagrams of the relative GTPase activity of human Rac1, yCdc73_C, yCdc73_full and BSA. The hRac1 and BSA act as the positive and negative control, respectively.



GTPase activity assay

GTPase activities were determined using the Innova Biosciences colorimetric ATPase assay system according to the manufacturer's recommendations (Product codes: 601-0120). This kit enables assay of reactions that generate Pi such as those catalyzed by ATPases and GTPases. Briefly, recombinant hRac1, yCdc73_C, yCdc73_full and the BSA (Negative control) were diluted to a final concentration approximately 10 μ M, respectively. 100 μ l Protein plus 100 μ l substrate (100 mM Tris (pH 7.5), 5 mM $MgCl_2$, 1 mM GTP) were carried out at 30 $^{\circ}$ C for 30 min. 50 μ l of Innova Biosciences Gold Mix (1:100 dilution of Accelerator into PiColorLock Gold) was added to the reaction mixture. Reaction mixtures were incubated for two minutes, after which 20 μ l of Stabilizer reagent was added. A635 readings were taken on SpectraMax M5 Microplate Reader system. Each experiment was repeated four times, and the average of the readings was taken in calculation.

Supplementary Table 1

Mutations in the C-terminal domain of hCdc73

Reference	Mutation	Codon	Predicted effect	Clinical manifestation ¹	Type
[Pimenta et al., 2006]	c.1124_1125dup	376	p.Asn376LeufsX10	sporadic OF	Germline
[Bradley et al., 2006]	c.1135G>A	379	p.Asp379Asn	HPT-JT	Germline
[Shattuck et al., 2003]	c.1231delC	411	p.Gln411ArgfsX17	sporadic PTC	Not Defined
[Carpten et al., 2002]	c.1239delA	413	p.Gln413HisfsX15	HPT-JT	Germline
[Pimenta et al., 2006]	c.1245_1262del	416	p.Gly416_Val421del	sporadic OF	Somatic
[Haag et al., 2008] ²	c.1432_1433del	478	p.Leu478GluX3	sporadic OF	Germline
[Wai Kwan Siu et al., 2011]	c.1475G>A	482	p.Trp492X	sporadic PTN	Germline

1. Clinical manifestation; OF ossifying fibroma; HPT-JT, hyperparathyroidism-jaw tumor syndrome; PTC, parathyroid carcinoma; PTN Parathyroid neoplasm with equivocal malignant potential.
2. Variant reported at british endocrine society meeting 2008 (endocrine abstracts [2008] 16 p 73).