Materials and Methods

Whole protein sequence datasets were retrieved from whole genome databases at jgi (http://genome.jgi-psf.org) (Grigoriev et al. 2012; Nordberg et al. 2014) and ncbi (for the sea squirt (*Ciona intestinalis*: Cion2), amphioxus (*Branchiostoma floridae*: Brafl1) from the jgi, sea urchin (*Strongylocentrotus purpuratus*) and acorn worm (*Saccoglossus kowalevskii*) from ncbi. Each of the Receptor Tyrosine Kinase and Cytoplasmic Tyrosine Kinase of the human genome were compared to these genomes using blastp (http://blast.ncbi.nlm.nih.gov/Blast.cgi) (Atschul et al. 1990). We used a threshold on the p-value of 1.0 e-20 and collected the 20 first best hits within each subfamilies. Non-vertebrates protein sequences were aligned using clustal omega (Sievers and Higgins 2014). Redundant sequences and sequences of non-vertebrate deuterostome with an incomplete Tyrosine Kinase domain were discarded. Phylogenetic trees were analyzed by Maximum Likelihood using PhyML v2.4.4 (Guindon et al. 2010). Methods with 1000 bootstrap iterations each. ML trees were run under a WAG model with estimated gamma distribution parameter. An additional selection was made on the CTK protein sequences that lack the transmembrane and the extra-cellular domains. A third selection was made on sequences that were not phylogenetically close to any human RTK were searched using blastp against the non-redundant metazoan database.

Additional Figure B. ML phylogeny based on the TK domain of the RTK sequences observed in human, sea squirt, amphioxus, sea urchin and acorn worm. For clarity, bootstrap values below 800 are not shown. Alternating colors allow to visualize the distinct subfamilies.

References

Altschul S, Gish W, Miller W, Myers E, Lipman D. 1990. Basic local alignment search tool. *J Mol Biol* **215**: 403-410.

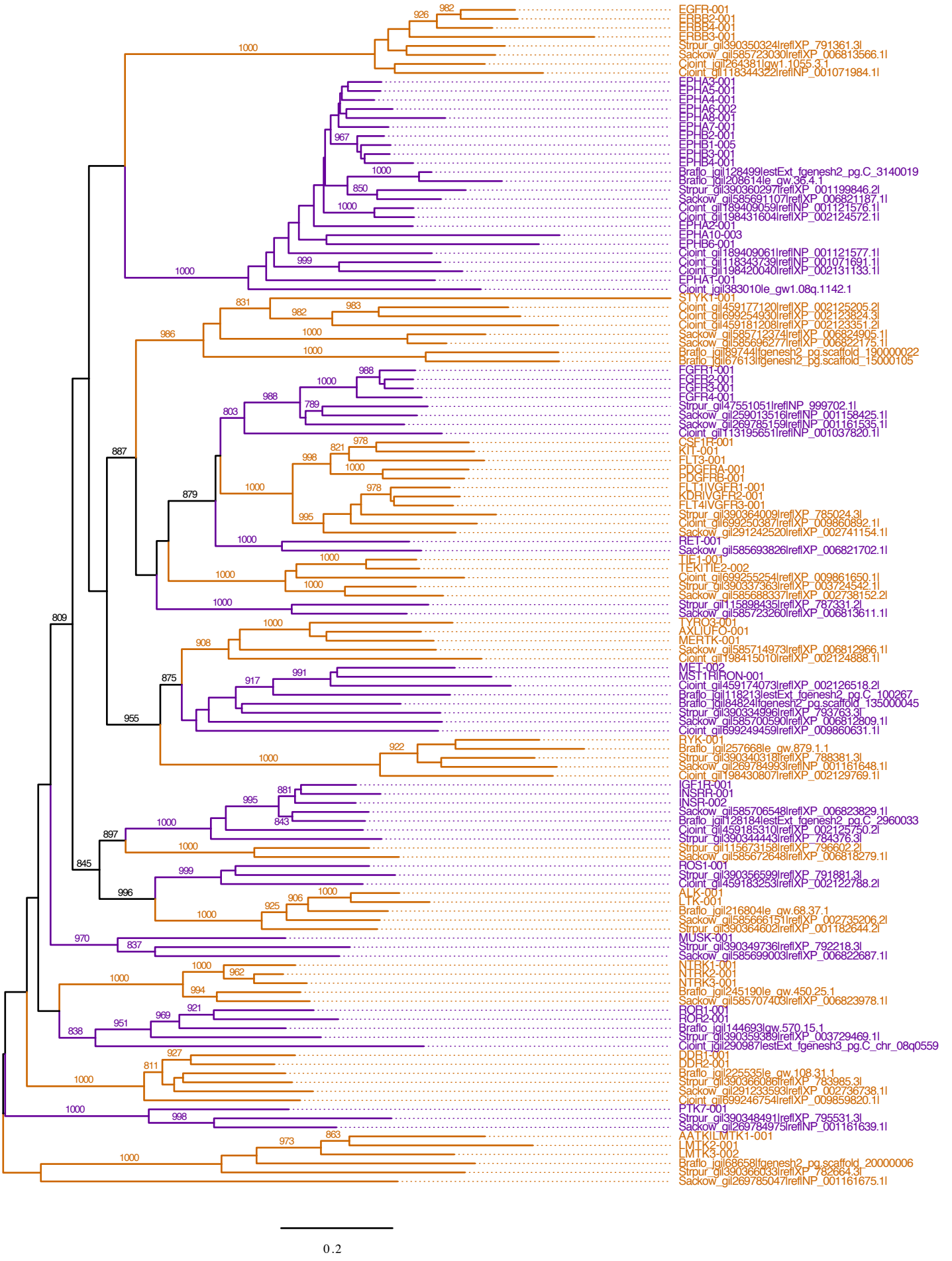
Grigoriev IV, Nordberg H, Shabalov I, Aerts A, Cantor M, Goodstein D, Kuo A, Minovitsky S, Nikitin R, Ohm RA, Otillar R, Poliakov A, Ratnere I, Riley R, Smirnova T, Rokhsar D, Dubchak I. 2012. The Genome Portal of the Department of Energy Joint Genome Institute. *Nucleic Acids Res* **40**:D26-32.

Guindon S, Dufayard JF, Lefort V, Anisimova M, Hordijk W, Gascuel O. 2010. New algorithms and methods to estimate maximum-likelihood phylogenies: assessing the performance of PhyML 3.0. *Syst Biol* **59**: 307-321.

Nordberg H, Cantor M, Dusheyko S, Hua S, Poliakov A, Shabalov I, Smirnova T, Grigoriev IV, Dubchak I. 2014. The genome portal of the Department of Energy Joint Genome Institute: 2014 updates. *Nucleic Acids Res* **42**:D26-31.

Putnam NH, Butts T, Ferrier DE, Furlong RF, Hellsten U, Kawashima T, Robinson-Rechavi M, Shoguchi E, Terry A, Yu JK, et al. 2008. The amphioxus genome and the evolution of the chordate karyotype. *Nature* **453**: 1064-1071.

Sievers F, Higgins DG. 2014. Clustal Omega, accurate alignment of very large numbers of sequences. Methods Mol Biol 1079: 105-116.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ERBB4-001
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Cioint_jgi|264381|gw1.1055.3.1
Cioint_gi|118344322|ref|NP_001071984.1|
EPHA3-001
EPHA5-001
EPHA4-001
EPHA6-002
EPHA8-001
EPHA7-001
EPHB2-001
EPHB1-005
EPHB3-001
EPHB4-001
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FLT4|VGFR3-001
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LMTK2-001
LMTK3-002
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