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Short communication

A novel homolog of protein tyrosine kinase Fyn identified in *Lampetra japonica* with roles in the immune response

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ABSTRACT

The non-receptor protein tyrosine kinase (nrPTK) Fyn, a member of the avian sarcoma virus transforming gene (Src) kinase family, plays a very significant role in cell growth, survival, apoptosis, tumor formation and immune response. In this study, a homolog of nrPTK Fyn was identified for the first time in the lamprey, *Lampetra japonica* and was named "Lja-Fyn". The cDNA fragment of lamprey *lja-fyn* contains a 1611-bp open reading frame, which encodes a protein of 537 amino acids. Multiple sequence alignment analysis showed that it shares four conserved domains (Src homology (SH) 4, SH3, SH2 and protein kinases catalytic domains) and a variable unique domain with vertebrates Fyn molecules. Though Lja-Fyn has high sequence similarity with typical Fyn and Yes molecules of jawed vertebrates, the identities among Lja-Fyn and typical Fyn molecules in unique domain are relatively higher than that among Lja-Fyn and typical Yes molecules. The result indicates that Lja-Fyn is a homolog of Fyn rather than Yes. The phylogenetic analysis showed that Fyn, Yes and Src molecules are grouped into three distinct phylogenetic clusters, and Lja-Fyn is grouped as a single branch in Fyn cluster. The real-time quantitative PCR assay revealed the wide distribution of the *lja-fyn* mRNA in lamprey immune related tissues. After stimulation with mixed antigens, the levels of *lja-fyn* mRNA were obviously up-regulated in the gill and lymphocyte-like cells, and the similar results were got by western blot analysis of Lja-Fyn protein expression. These results indicated that nrPTK Lja-Fyn was likely to be involved in immune response. Furthermore, our present findings also provide the necessary information for understanding the distinction between lamprey Lja-Fyn and other members of jawed vertebrates in Src family.

1. Introduction

Protein phosphorylation is one of the basic ways for intercellular signal transduction, and this process is catalyzed by different protein kinases in the cells (Johnson and Lewis, 2001).Tyrosine protein kinases (TPKs) is a group of these main protein kinases, and their phosphorylation sites are the tyrosine residues of other proteins. The TPKs can be divided into two subgroups, receptor tyrosine protein kinases (rTPKs) and non-receptor tyrosine protein kinases (nrTPKs) (Hanks et al., 1988). The Src-family kinase (SFK), which is composed of nine members, is a family belonging to nrTPKs. The SFKs are found to be involved in a wide range of signaling pathways at the plasma membrane, resulting in cell proliferation, differentiation, migration, and cell-shape changes (Thomas and Brugge, 1997). The SFKs can be divided into three subfamilies based on their conserved protein domains: SrcA subfamily (Src, Yes, Fyn and Fgr), SrcB subfamily (Lck, Hck, Blk, and Lyn) and Frk subfamily (Lowell, 2004). Nearly all SFKs except Frk contain an N-terminal Met-Gly-Cys consensus sequence locating in a Src homology (SH) 4 domains. The SH4 domain contains 10 amino acids and can promote dual fatty acylation with myristate and palmitate, which play a significant role in making the Src protein anchor to the inner surface of the cell membrane (Alland et al., 1994; Liang et al., 2001). An intrinsically disordered segment containing 60–90 residues locates following the SH4 domain. The segment is called unique domain (UD) for the reason that it exhibits strong sequence divergence among SFK members. The interplay between various phosphorylation sites within the UD emphasizes its role as a signaling integration hub (Amata et al., 2014). Two highly conserved consecutive domains (SH3 and SH2 domains) are next to the UD and at the upstream of the protein kinases catalytic (PKC) domain. The SH3 domain can bind to proline-rich sequences and the SH2 domain makes SFKs interact with tyrosine phosphorylated residues (Brown and Cooper, 1996). The PKC domain catalyzes phosphor transfer reaction through its big and small lobes that bind protein substrates

Abbreviations: Fyn, Proto-oncogene tyrosine-protein kinase Fyn; Lja-Fyn, Fyn-like of *Lampetra japonica*; RACE, Rapid Amplification of cDNA Ends; qPCR, Real-time quantitative PCR detecting system; Src, Proto-oncogene tyrosine-protein kinase Src; Yes, Yamaguschi sarcoma virus gene; Fgr, Gardner–Rasheed feline sarcoma viral (v-fgr) oncogene homolog; Lyn, Lck/Yes-related novel protein tyrosine kinase; Lck, Lymphocyte-specific protein tyrosine kinase; Blk, B lymphocyte kinase; Hck, Hematopoietic Cell Kinase; Yrk, Yes-related kinase; Tec, Tyrosine kinase expressed in hepatocellular carcinoma.

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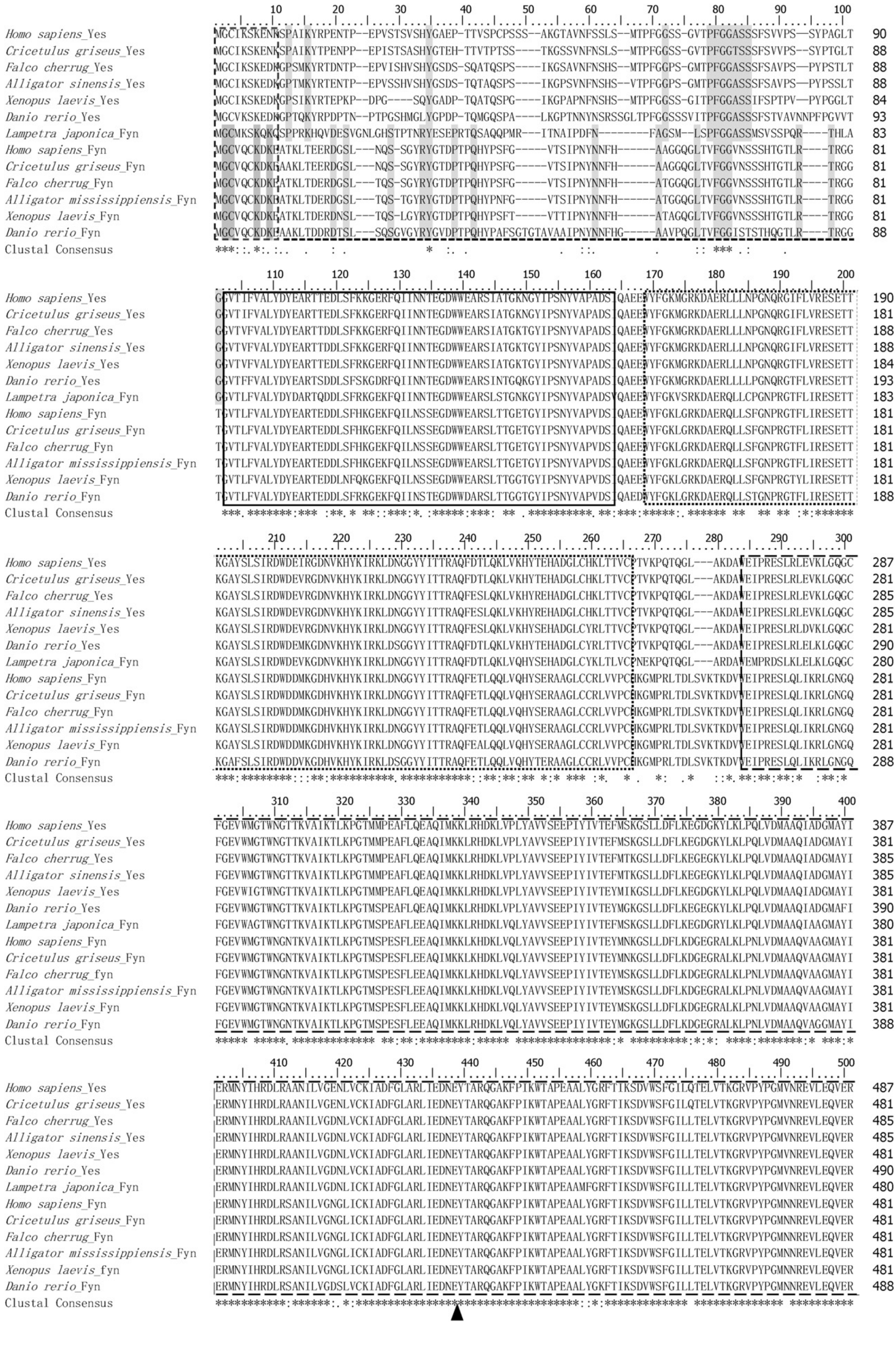
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