Structure, evolution and expression of collagen XXVIII: Lessons from the zebrafish

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Abstract

Collagen XXVIII is the last discovered member of the collagen superfamily and thus has been only sparsely investigated. We studied collagen XXVIII in zebrafish to gain insight into its structure, evolution and expression. In contrast to human and mouse, the zebrafish genome contains four collagen XXVIII genes, *col28a1a* and *-b*, and *col28a2a* and *-b*. Genomic context and phylogenetic analysis revealed that the *a2* branch was lost during evolution of mammals, whereas the duplication of the *a1* and *a2* branches results from the whole genome duplication in the teleost lineage. Sequence analysis revealed conservation of domain structure and the unique imperfections in the triple helical domain. Two major forms of collagen XXVIII were identified, Col28a1b in adult and Col28a2a in 3–5 dpf zebrafish. Composite agarose/polyacrylamide gel electrophoresis revealed that both these chains mainly form dimers of trimers, although Col28a1b appears to be more polydisperse. Homodimers are abundant, although it is possible that complexes consisting of Col28a2a and Col28a1a or -a2b occur. Peptide mass fingerprint analysis revealed that the C-terminal Kunitz domain is often proteolytically processed. In contrast to murine collagen XXVIII, the zebrafish orthologs are widely expressed and not only present in the nervous system. They are differentially expressed in the liver, thymus, muscle, intestine and skin. Altogether our results point to a unique nature of collagen XXVIII within the collagen family.

Introduction

The collagen superfamily is a heterogeneous group of proteins with many *in vivo* functions. Its members play important roles in tissue formation, stability and maintenance (*e.g.* cell adhesion, migration, differentiation, and wound healing), for review see [1]. To date 28 different collagens are known which are encoded by 46 different genes. The protein family can be subdivided into fibril, beaded filament, anchoring fibril, and network forming collagens. Structurally, collagens are defined by their Gly-X-Y repeats where X and Y are often a proline or hydroxyproline residue leading to the formation of left-handed polyproline II helices that assemble into twisted, tightly packed right-handed triple helices. However, many collagens also contain non-collagenous domains and depending on the individual domain structure they can form very different supramolecular assemblies.

Information about collagen XXVIII is sparse, knockout or knockdown models are not available and it is not clear if this collagen belongs to one of the four collagen subgroups or if it is unique. The human and murine proteins consist of an N-terminal VWA (von Willebrand factor type A) domain followed by a 528 amino acid residue collagenous domain, which has altogether 16 uniformly arranged, very short imperfections (G1G and G4G) in the Gly-X-Y repeat, unique among the known collagens [2]. The C-terminus is made up by a second VWA domain followed by a unique domain and a domain related to the BPTI/Kunitz family of serine protease inhibitors

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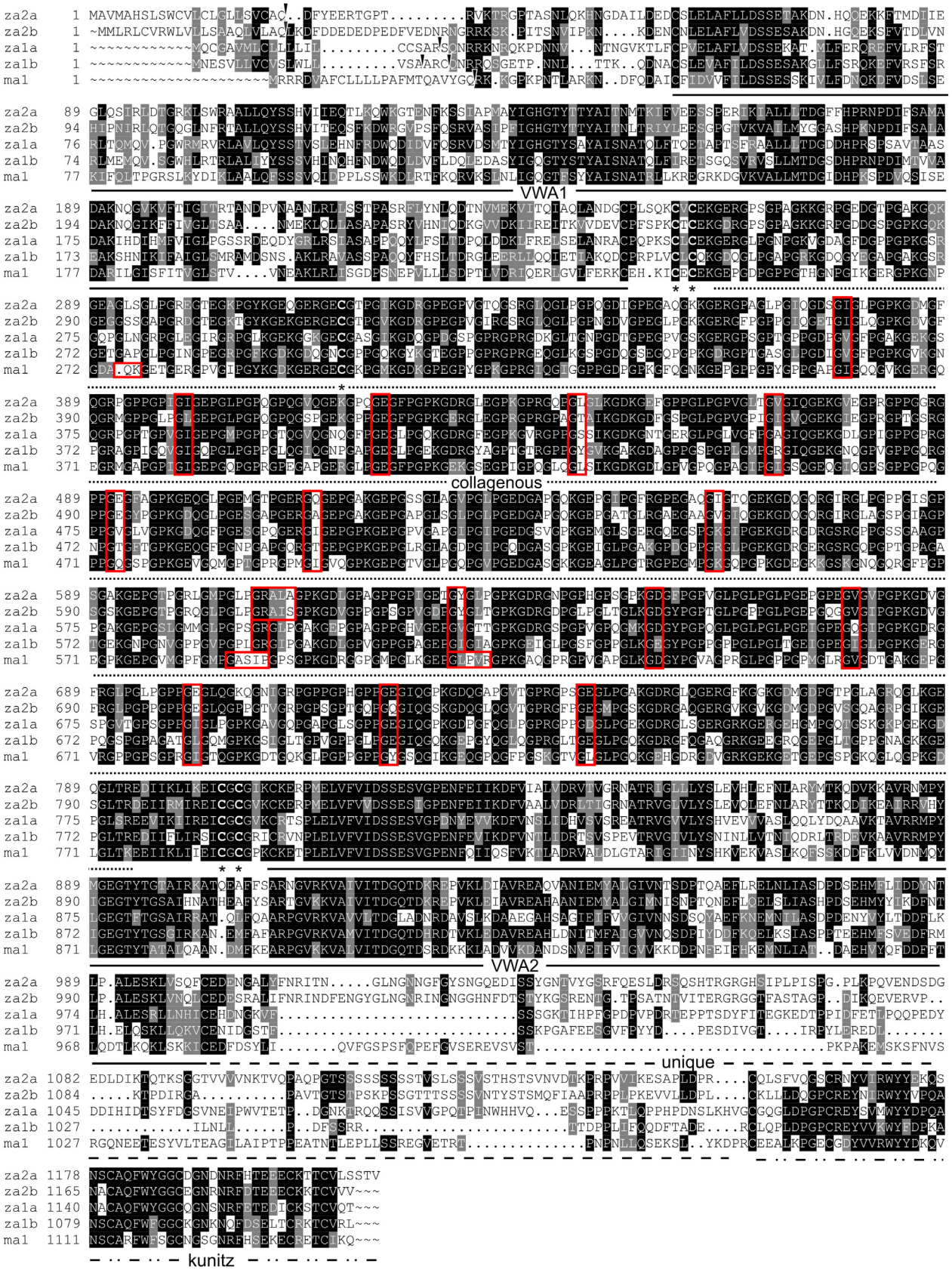

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