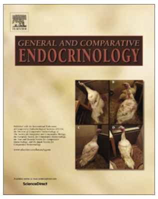
General and Comparative Endocrinology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

General and Comparative Endocrinology

journal homepage: www.elsevier.com/locate/ygcen



Review

Role of elasmobranchs and holocephalans in understanding peptide evolution in the vertebrates: Lessons learned from gonadotropin releasing hormone (GnRH) and corticotropin releasing factor (CRF) phylogenies

David A. Lovejoy *, Ola M. Michalec, David W. Hogg, David I. Wosnick

Department of Cell and Systems Biology, University of Toronto, Toronto, Ontario, Canada

ARTICLE INFO

Article history:
Received 6 July 2017
Revised 6 September 2017
Accepted 13 September 2017
Available online xxxx

Keywords:
Chondrichthyes
Evolution
Vertebrates
Metabolism
Stress
Reproduction

ABSTRACT

The cartilaginous fishes (Class Chondrichthyes) comprise two morphologically distinct subclasses; Elasmobranchii and Holocephali. Evidence indicates early divergence of these subclasses, suggesting monophyly of their lineage. However, such a phylogenetic understanding is not yet developed within two highly conserved peptide lineages, GnRH and CRF. Various GnRH forms exist across the Chondrichthyes. Although 4–7 immunoreactive forms have been described in Elasmobranchii, only one has been elucidated in Holocephali. In contrast, Chondrichthyan CRF phylogeny follows a pattern more consistent with vertebrate evolution. For example, three forms are expressed within the lamprey, with similar peptides present within the genome of the *Callorhinchus milii*, a holocephalan. Although these findings are consistent with recent evidence regarding the phylogenetic age of Chondrichthyan lineages, CRF evolution in vertebrates remains elusive. Assuming that the Elasmobranchii and Holocephali are part of a monocladistic clade within the Chondrichthyes, we interpret the findings of GnRH and CRF to be products of their respective lineages.

1. Introduction

Reproduction is essential for the continuity of species. In chordates, gonadotropin-releasing hormone (GnRH) is the apical neuronal hormone for the regulation of reproduction. However, the process of reproduction is an energy-intensive endeavor and can be compromised by stress-related events such as predation, mate acquisition, and nutritional foraging. As a result, a complex physiological stress-response system has evolved in chordates to ensure reproduction and survival under stressful conditions (Lovejoy and Barsyte-Lovejoy, 2010). Because the neuroendocrine stress response is primarily regulated by corticotropin-releasing factor (CRF), GnRH and CRF work in conjunction with one another to ensure the survival of and reproduction of chordates.

Both peptides are found within a family of paralogous forms in chordates. Understanding the evolution and phylogeny of these peptides is essential to determine how each respective chordate lineage has developed the capacity to reproduce under life-threatening situations. Although there is an excellent understanding of the expression of GnRH and CRF paralogues in agnathan fishes, and in phylogenetically younger vertebrate lineages such as lobe-finned fishes, ray-finned fishes and tetrapods, there is scarce information on the expression and identity of GnRH and CRF paralogues in cartilaginous fish species. The cartilaginous fish (Chondrichthyes: chimeras, sharks, skates and rays) are the extant representatives of the first jawed fishes. Due to their ancestral nature, Chondrichthyes occupy an evolutionary position between the jawless fishes (agnathans) and the lineages that radiated into both the tetrapods and lobe-finned fishes (Sarcopterygii) as well as the ray-finned fishes (Actinopterygii).

In this review, we examine the expression of GnRH and CRF in the cartilaginous fishes to understand the development of paralogy in the context of these lineages.

2. Phylogeny of the cartilaginous fishes

The cartilaginous fishes, (class Chondrichthyes) comprise sharks, skates, rays and chimaeras, and represent the extant manifestation of the first jawed fishes that evolved some 450 million years ago. The formation of jaws and the associated predatory

---

* Corresponding author at: Department of Cell and Systems Biology, 25 Harbord Street, University of Toronto, Toronto, Ontario M5G 3G5, Canada.

E-mail address: david.lovejoy@utoronto.ca (D.A. Lovejoy).

https://doi.org/10.1016/j.ygcen.2017.09.013
0016-6480/Crown Copyright © 2017 Published by Elsevier Inc. All rights reserved.

Please cite this article in press as: Lovejoy, D.A., et al. Role of elasmobranchs and holocephalans in understanding peptide evolution in the vertebrates: Lessons learned from gonadotropin releasing hormone (GnRH) and corticotropin releasing factor (CRF) phylogenies. Gen. Comp. Endocrinol. (2017), https://doi.org/10.1016/j.ygcen.2017.09.013

behaviour were pivotal in the evolution and success of their phylogenetically later vertebrate descendants. The Chondrichthyes consist of two morphologically distinct subclasses (Fig. 1). The Elasmobranchii include the sharks, skates and rays, whereas the Holocephali consist of only the chimaeras (ratfishes, elephant fishes, and rabbit fishes). Over the last century, debate has persisted whether the two subclasses possess a single ancestor, indicative of a monophyletic clade (Coates et al., 2017; Maisey, 2012; Inoue et al., 2010; Li et al., 2012). Debate also continues regarding a polyphyletic origin of the Chondrichthyes and which lineage would have evolved first (Gillis et al., 2011; Pradel et al., 2011). Despite opposition, there is general agreement that the two subclasses diverged at an early stage of their respective origins about 440 million years ago (Maisey 2012; Grogan and Lund, 2000; Renz et al., 2013) and the Holocephali may possess traits that provide a transitional situation between jawless (Agnathans) and jawed fishes (Gnathostomes) (Coates et al., 2017). However, regardless of the monophyletic or polyphyletic origin of the Chondrichthyes, the early divergence of the two subclasses has provided sufficient evolutionary time for the development of numerous derived traits. Thus, we will not attempt to review the data on the monophyly or polyphyly of the Chondrichthyes, but rather focus on what is known and, importantly, what is not known about two key peptide systems that are essential for successful reproduction (GnRH) and responding to stressful challenges (CRF).

First, the Holocephali represent a small subclass of the Chondrichthyes and consists of around 40 species (Inoue et al., 2010) (Fig. 2). Classified within a single order, Chimaeriformes, they comprise two lineages including the elephant-fishes (Callorhinchus; termed 'elephant shark' in recent publications) and the rat- and rabbit-fishes (Hydrolagus, Chimaera, Rhinochimaera for example). The second subclass, the Elasmobranchii, consists of over 800 species and can be divided into two lineages. Included are the Selachii (sharks and rays) and the Batoidea (rays and skates), which may be a sister lineage to the Squalomorph sharks on one lineage and Galeomorph sharks on the other lineage (Vélez-Zuazo and Agnarsson, 2011; McEachran and Aschliman, 2004), though other relationships have been suggested (Benton and Donoghue, 2006; Nelson, 2006). We will not attempt to provide a rationale for GnRH and CRF evolution to fit within any of the reported phylogenies, but rather will use this simply to provide a framework for the expression of these peptides within existing phylogenetic schemes.

3. Genome duplications in vertebrates

The understanding of genome duplications in chordates has been instrumental in providing a foundation upon which to base our identification of peptide orthologues and paralogues. Termed the '2R' hypothesis, this theory posits that after the formation of the protochordates, the basal chordates underwent two rounds of genome duplication leading to an expansion of paralogous gene formation as typically seen in extant chordates. Thus, if a single gene was present in a protochordate, then four paralogous genes should be present in later-evolving chordates. In species or lineages that have less than four genes, this is presumably indicative of the loss of additional genes. Moreover, those groups that show a greater than four presence of a given gene homologue suggests additional gene duplication. Among vertebrates, additional gene or genome duplication events, after the original 2R event, has been suggested for Chondrichthyes (Robinson-Rechavi et al., 2004), bony fish (Opazo et al., 2012) and amphibians (Liang et al.,

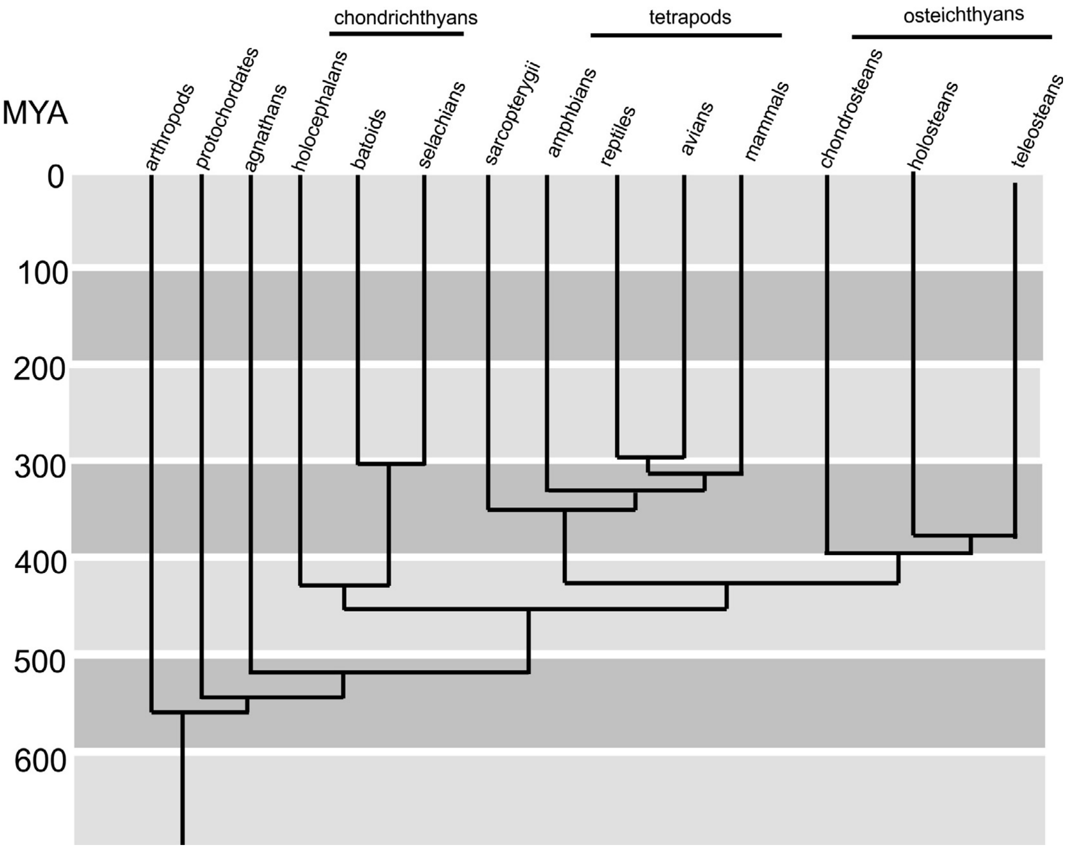


Fig. 1. Phylogeny of chordates and vertebrates. The cartilaginous fishes (Chondrichthyes) represent the extant manifestation of the first jawed vertebrates. See text for detailed discussion.

Please cite this article in press as: Lovejoy, D.A., et al. Role of elasmobranchs and holocephalans in understanding peptide evolution in the vertebrates: Lessons learned from gonadotropin releasing hormone (GnRH) and corticotropin releasing factor (CRF) phylogenies. Gen. Comp. Endocrinol. (2017), https://doi.org/10.1016/j.ygcen.2017.09.013