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CECR 1

Which Came First: Parathyroid Hormone or Parathyroid Hormone-Related Protein?

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Human chromosomes 11 and 12, which have parathyroid hormone (PTH) and parathyroid hormone-related protein (PTHrP) on their respective short arms, are known to have arisen through an ancient gene duplication event.[1] Every species from sharks through to man has at least one of each of the genes for PTH and PTHrP. In some of the fish species, multiple genes for both PTH and PTHrP have been identified. The phylogenetic analysis indicates that in the elephant shark (*Callorhinchus milii)* the point where the duplication resulting in these genes took place is close. There were two copies of the PTH gene in elephant sharks and these have not persisted in higher vertebrates indicating that one of these PTH genes has accumulated a number of deleterious mutations and has been lost in the process. The recent sequencing of the Japanese lamprey genome (*Lethenteron japonicum*)[2] is instructive. Jawless fish (lampreys and hagfish) have a pivotal position in evolutionary history, having undergone two whole genome duplications when compared with invertebrates. Like sharks, they have a cartilaginous skeleton but have the ability to move from seawater to freshwater. Whole genome duplications affect the animal's entire set of genes simultaneously and after the duplication one copy of the gene may be lost or acquire a new function. The Japanese lamprey genome database has been interrogated for the presence of *PTH* and *PTHrP*. Also tissues from the Japanese lamprey were examined for the expression of these genes. Certainly two receptors for PTH and PTHrP (*pth1r* and *pth2r*) are present in agnathan genome (*Petromyzon marinus)*.[3] Two PTH receptors have also been identified in invertebrates (*Ciona intestinalis*) but the ligands have not been found.[4] The evolutionary history of PTH and PTHrP might indicate which of these genes was the original gene and what possible novel roles each of the proteins/hormones may have.

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Calcium Regulation in Egg-Laying Chickens

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Chicken calcium metabolism in an egg-laying period is extraordinary when compared with all other classes of vertebrates, since the egg-laying hens produce up to three hundred eggs with hard-eggshell per a year. The eggshell consists of 5.7 g calcium carbonate ($CaCO_3$) containing about 2.3 g of net calcium. About 60-75% of the calcium in the eggshell is derived from dietary sources and the remaining of 25-40% from skeletal stores, called "medullary bone". Medullary bone is specifically developed in marrow cavities of long bones and plays an important role as a calcium reservoir for eggshell formation. There are osteoblasts, osteoclasts on medullary bone surface, as well as osteocytes embedded in the matrix. In the domestic hens, medullary bone formation and resorption occur alternately during the 24-hour egg-laying cycle. These cyclic changes in medullary bone metabolism depend on the site of an egg in the oviduct. Namely, when an egg is in the infundibulum, magnum and or isthmus of the oviduct, osteoblasts actively form medullary bone. On the other hand, when an egg enters into the shell gland and begins to be calcified, osteoclasts resorb medullary bone and mobilise calcium for eggshell formation. It has been reported that osteocytes play a key role for bone formation and resorption. However, the function of medullary bone osteocytes is still unknown. We have recently observed that carbonic anhydrase II (CAII) is localised in medullary bone osteocytes. CAII is a known proton generator which lyses calcified matrix, and is expressed in osteoclasts. In contrast to medullary bone osteocytes, cortical bone osteocytes do not contain carbonic anhydrase. These results suggest that osteocytes may also resorb medullary bone for eggshell formation.

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