

## Ghrelin May Be a Universal Peptide in all Living Organisms

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Ghrelin (GAH) (1) is a new gastrointestinal hormone discovered from the rat stomach in 1999 by Kojima et al. (2). This peptide bears 19-28 amino acids and its third amino acid is usually a serine but in some species a threonine is modified by an acyl acid (3,4). In this respect, ghrelin is the first known example of a peptide modified by a fatty acid (3,4). Two major forms of GAH are present in tissues and blood: des-acylated (dGAH (inactive)) and octanoylated (aGAH (active)) (1-4). The activity of desacylated ghrelin does not require binding to the growth hormone secretory receptor-1a (GHSR-1a) (4), and can cross the blood-brain barrier (5), but in terms of appetite stimulation the "active" form may be more physiologically important.

Synthesis of ghrelin (lipopeptide hormone) occurs mainly in the stomach (2-4), with smaller amounts produced in the salivary glands, placenta, kidney, pituitary, central nervous system, heart, parathyroid glands, small intestine, pancreas, hypothalamus (reviewed (3,4)), and breast (6). GAH mRNA has been reported in other tissues as well (7). More recent research in our laboratory showed that a GAH-like substance is also present in plants (8).

A number of studies have shown that ghrelin (lipopeptide hormone) has multiple effects other than on growth hormone (GH) secretion, including gastrointestinal coordination, energy metabolism, facilitation of cell survival and proliferation, inhibition of apoptosis, and regulation of food intake (4). N-octanoyl-homoserine lactone is a widespread example of the cell-cell signaling molecules that are involved in food-searching and other physiological responses in gram-negative bacteria, and it has been suggested that the structural homology between this molecule and the active form of GAH (O-acylation of serine) may indicate evolutionary convergence (9).

Here I hypothesize that ghrelin or ghrelin-like substances are universally present in all living organisms, including plants and the microbial world (viruses, protists, archaeobacteria, photosynthetic eubacteria, and so on). Supporting this notion, a ghrelin-like substance in plants (8), and serine acetyltransferase gene family in *Arabidopsis thaliana* (9) as well as n-octanoyl-homoserine lactone, a structural homologed with active form of ghrelin in gram-negative bacteria (10), were present other than in the animal world (3,4). As hypothesized here, if ghrelin is present in all living organisms, it might play a crucial role in cell division and food searching, and life cannot progress without ghrelin, not only in eukaryotic cells but also in prokaryotic cells. This issue warrants further studies.

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