

## ABSTRACT OF DISSERTATION

Title	<p>Long-term administration of whey alters atrophy, gene expression profiles and dysfunction of salivary glands in elderly rats (ホエーの長期間摂取が老齢ラット唾液腺の萎縮、遺伝子変化、機能低下に及ぼす効果)</p>
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<p>A decline in the function of salivary glands, associated with aging is considered to reduce the quality of life by disrupting the normal homeostasis of the oral cavity and increasing the risk of oral and systemic diseases. A number of studies have considered whey, a natural by-product of cheese making process, as a source of valuable constituents that possess important nutritional and biological properties – particularly with regard to prevention of diseases and promotion of health during aging.</p> <p>In the present study we examined the effects of whey supplementation on age-related changes in morphology, gene expression and function of rat salivary glands. Long-term (4-week) administration of whey prevented and/or restored age-dependent decline of salivary volume, protein concentration and atrophy of sublingual glands (SLGs) in 88-week-old rats. Western blot analysis confirmed quantitative changes in levels of selected proteins in the SLGs and saliva in response to whey administration. The transcripts of 42 genes were up-regulated and 7 genes were down-regulated by more than 1.5-fold change with <math>FDR \leq 0.1</math> after whey-drinking. The expression levels of genes associated with salivary proteins, tissue repair, salivary gland homeostasis and development were significantly increased, while those associated with lipid metabolism, signal transduction, cancer and senescence were decreased. Overexpression of transcription factor activating protein 2 beta (<i>Tcfap2b</i>) and androgen-binding protein alpha (<i>Abpa</i>), as well as presence of Ap-2 binding sites and androgen response elements in the promoter regions of almost all genes altered after whey administration, suggesting that androgen-dependent transcription programmes functioned together with a tissue-specific collaborating factor AP-2 in sublingual glands of whey-drinking rats.</p> <p>This is the first study to report that whey-administration can prevent and/or restore age dependent atrophy and functional decline of SLGs in relation to gene expression and thus may serve as a functional food ingredient.</p>	