【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Medicine, dentistry, and pharmacy Ⅱ)

Title of Project：KLF network in chronic diseases and cancer

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Research Area：Medicine, dentistry, and pharmacy

Keyword：Molecular vascular biology

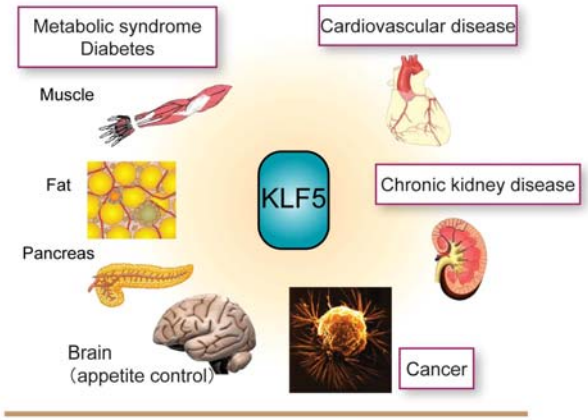
【Purpose and Background of the Research】

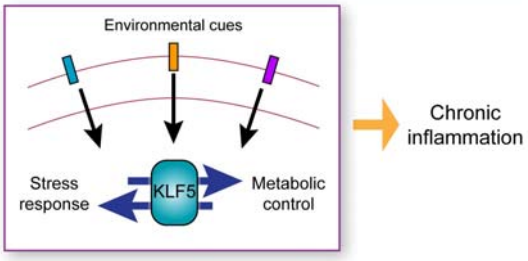
The Krüppel-like factor family consists of 17 zinc-finger-type transcription factors. KLFs are known to play important roles in development, cell differentiation, stem cells, and various diseases. KLF4 is required for induction of iPS cells.

We have demonstrated that KLF5 is one of the key molecules involved in development of cardiovascular disease and metabolic syndrome. Recently, we found that KLF5 also plays a role in chronic kidney disease. Members of the KLF family are suggested to interact with each other.

In this project, we will analyze the transcription factor networks that control initiation and development of cardiovascular, renal and metabolic diseases, and cancer. In particular, we will focus on KLFs, such as KLF5. Our study aims to elucidate the common pathological mechanisms underling chronic diseases. We will also develop novel therapeutic strategies against the molecular mechanisms.

【Research Methods】





We will analyze the functional roles of KLF5 and other KLF members in cardiovascular, renal, and metabolic diseases, and cancer using technologies, such as tissue-specific genetically altered mice. We will elucidate the common molecular mechanisms underling those various diseases. We will focus on cardiac hypertrophy, heart failure, chronic kidney disease, metabolic syndrome, diabetes, and cancer.

【Expected Research Achievements and Scientific Significance】

Results of our previous studies strongly suggest that KLF5 is a key molecule for development of various diseases, including cardiovascular and metabolic diseases, and cancer. Our study is aim to elucidate the common pathological mechanisms underling chronic diseases and cancer. Our study would also lead to development of novel therapeutic strategies against the common pathogenic mechanisms.

【Publications Relevant to the Project】

· Takeda N, Manabe I, Uchino Y, Eguchi K, Matsumoto S, Nishimura S, Shindo T, Sano M, Otsu K, Snider P, Conway SJ, Nagai R. Cardiac fibroblasts are essential for the adaptive response of the murine heart to pressure overload. ***J Clin Invest*** 120:254-265, 2010.

· Nishimura S, Manabe I, Nagasaki M, Eto K, Yamashita H, Ohsugi M, Otsu M, Hara K, Ueki K, Sugiura S, Yoshimura K, Kadowaki T, Nagai R. CD8+ effector T cells contribute to macrophage recruitment and adipose tissue inflammation in obesity. ***Nat Med*** 15:914-920, 2009.

· Oishi Y, Manabe I, Tobe K, Ohsugi M, Kubota T, Fujiu K, Maemura K, Kubota N, Kadowaki T, Nagai R. SUMOylation of Kruppel-like transcription factor 5 acts as a molecular switch in transcriptional programs of lipid metabolism involving PPAR-[delta]. ***Nat Med*** 14:656-666, 2008.

【Term of Project】 FY2010-2014

【Budget Allocation】 167,400 Thousand Yen

【Homepage Address and Other Contact Information】 http://plaza.umin.ac.jp/nagai