

MCM Update - May 2024: KLF5

Terminology

- **Transcription factor:** A protein that controls the rate of transcription from DNA to RNA, by binding a particular sequence of DNA.
- **Transcription:** The process by which an RNA copy is made from a DNA sequence.
- **Promoter elements:** The DNA region where transcription is initiated.
- **Sphingolipid:** A type of lipid that contains a backbone spingoid base.
- **Trophoblast:** A layer of cells that helps a developing embryo attach to the uterus, protects the embryo, and forms part of the placenta.
- **Diabetic neuropathy:** Nerve damage that is caused by diabetes.
- **Diabetic cardiomyopathy:** Changes in heart muscle tissue's structure and function caused by diabetes.
- **Lupus nephritis:** Kidney disease caused by lupus, an autoimmune disease.
- **Chronic obstructive pulmonary disease (COPD):** A group of diseases that cause airway blockage and breathing-related problems.

Summary

We continue to characterise lung cancer biomarkers identified in the MCM1 project. This update focuses on KLF5, a well-studied gene that has been implicated in several cancer types. KLF5 is a transcription factor, which is expressed across numerous organs and tissues.

Background

Identifying molecular markers and their combination (signatures) enables us to detect disease earlier (diagnostic signatures) and stratify patients into subgroups based on disease progression patterns (prognostic signatures). The final group of markers helps identify which patients will benefit from specific treatment options (predictive signatures). The Mapping Cancer Markers project analyses data sets with millions of data points collected from patients with cancers to find such diagnostic, prognostic and predictive signatures.

Since November 2013, World Community Grid volunteers have donated over 901,000 CPU years to the project, helping analyse data on lung and ovarian cancer and sarcoma, much more thoroughly than otherwise possible. We are immensely grateful for this continued support.

Focusing on characterising the 26 top-scoring genes in lung cancer, we have already discussed [VAMP1](#), [FARP1](#), [GSDMB](#), [ADH6](#), [IL13RA1](#), [PCSK5](#), [TLE3](#), and [HSD17B11](#) in previous MCM updates. Here, we outline information on KLF5.

KLF5 Research

KLF5 (Krueppel-like factor 5) is a transcription factor that activates the transcription of multiple genes ([Uniprot](#)). The importance of KLF5 in lung cancer is further strengthened since it also targets genes we have already discussed: VAMP1, IL13RA1, PCSK5 and TLE3.

KLF5 has been implicated in diverse biological processes, blood vessel remodelling^[1] and maintenance^[2], sphingolipid metabolism and skin barrier function^[3], cell response to stress^[4,5], tooth formation in mice^[6], embryo and trophoblast differentiation^[7,8,9], skeletal muscle differentiation^[10], and stem cell self-renewal^[9,11]. KLF5 is expressed across many organs and tissues (Figure 1). Studies have also suggested that KLF5 may be implicated in conditions such as diabetic nephropathy^[12] and cardiomyopathy^[13], renal fibrosis in lupus nephritis^[14], protection from immune response in colitis^[15], and airway inflammation in asthma^[16].

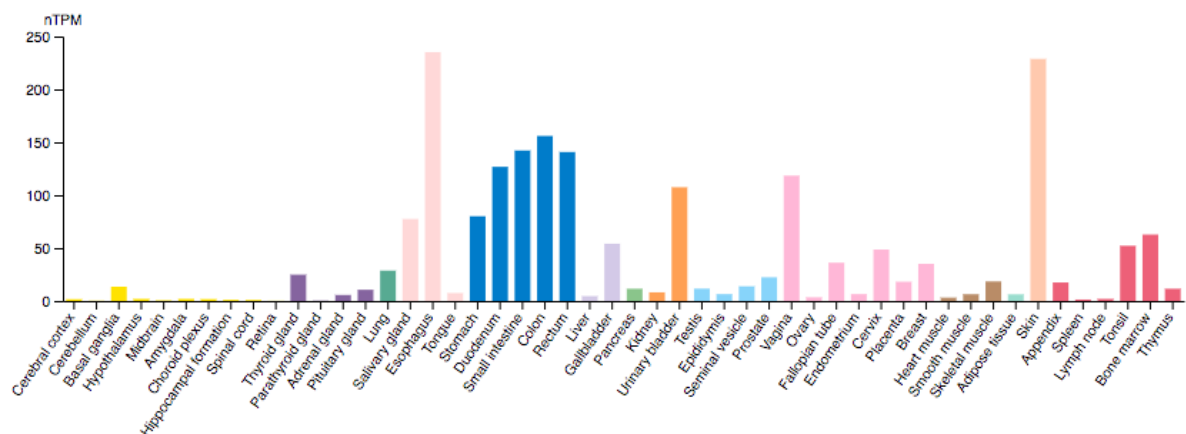


Figure 1. KLF5 expression across different tissue types ([Human Protein Atlas](#)).

KLF5 is also upregulated in the airways of patients with chronic obstructive pulmonary disease (COPD) and may be involved in tissue remodelling in COPD^[17]. Notably, studies have demonstrated that COPD and lung cancer are closely linked at a molecular level^[18].

As was the case with the other genes we have presented so far, KLF5 was found to have a protective role in lung cancer (Figure 2A), which is especially strong for non-smokers (Figure 2B).

P value: 0.0132

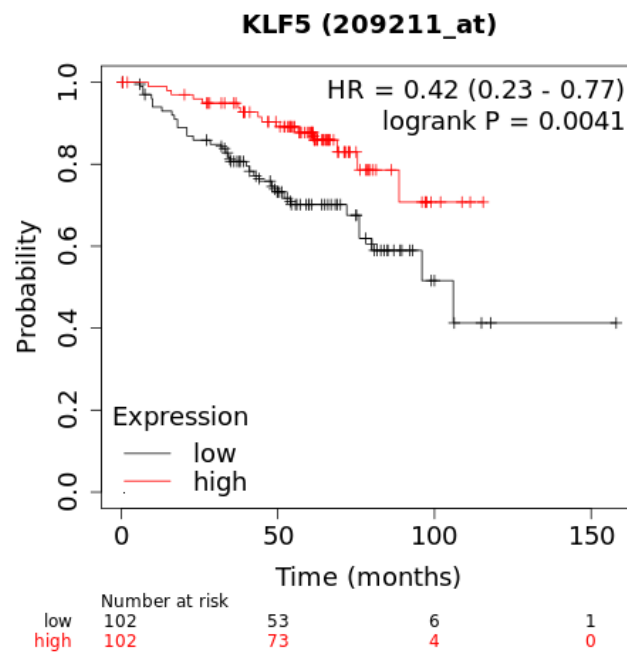
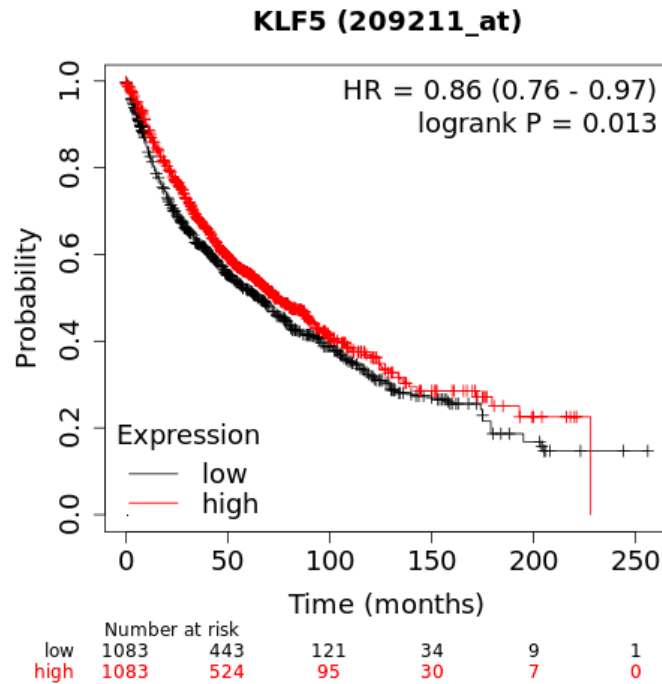


Figure 2. (A) Survival curves for lung cancer patients with low and high expression of KLF5 ([KMplot](#)), and (B) for non-smoking patients only.

We have also explored the association between KLF5 and other cancers. As shown in Figure 3, comparing cancer tissues with normal tissues, KLF5 is differentially expressed in all but one cancer examined (indicated by red text). Notably, KLF5 is upregulated in lung cancer as well as most other cancers, while it is downregulated in only 7 of the 22 cancers examined. Within the literature, KLF5 has a well-studied association with numerous cancer types, including ovarian cancer^[19], stomach

cancer^[20], esophageal cancer^[21], thyroid cancer^[22], prostate cancer^[23], endometrial cancer^[24], pancreatic cancer^[25], and recently also in lung cancer^[26].

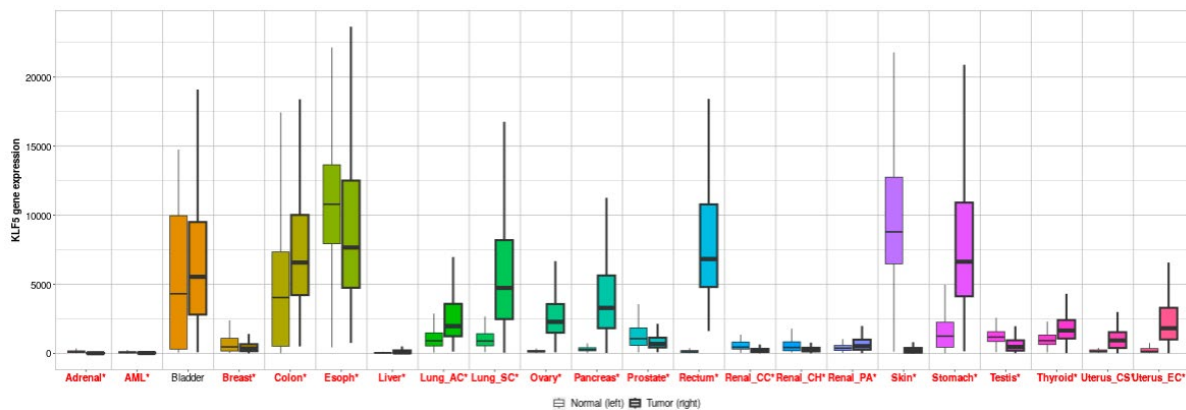


Figure 3. Expression of *KLF5* in normal and cancer tissue for multiple cancer types. Red text represents a significant difference between expression in cancer tissue compared with normal tissue ([TNMplot](#)).

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