Somatic Loss of Heterozygosity as a Driver in Fumarate Hydratase Deficient Renal Cell Carcinoma

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Background

- Fumarase Hydratase Deficient Renal Cell Carcinoma (FH-RCC) is a rare and aggressive form of kidney cancer linked to bi-allelic inactivation of the *FH* gene.
- *FH* inactivation alone is not enough for cancer development. However, other factors which contribute to tumor formation remain under studied.
- Our research aims to identify germline variants in well known cancer-associated genes for LOH.

Key Terms

Bi-allelic Inactivation: Loss of function of both alleles of a gene resulting from one or more alterations.

Loss of Heterozygosity (LOH): Somatic mutation causing alleles to become homozygous.

Cancer Driver: Genes that promote the formation and development of Cancer.

Findings

- *FH* & *PCSK9* are the only driver genes with evidence of LOH at heterozygous loci.
- Our observation of LOH in *FH* supports past research on cancer formation through germline variants.
- Other cancer associated drivers present no evidence of LOH in patients with FH-RCC.

Future Direction

- Understanding the role, if any, played by *PCSK9* in FH-RCC tumor development.
- Further exploration of clinical properties and treatment responsiveness of cancers presenting LOH.

Methods

Sample Collection → Whole Genome Sequencing → Sequence Alignment → Identify Germline / Somatic Variants → Assess B-allele Frequencies → Clinical Correlation

Results

Figure 1: Tumor *vs.* Normal B-allele Frequency By Gene

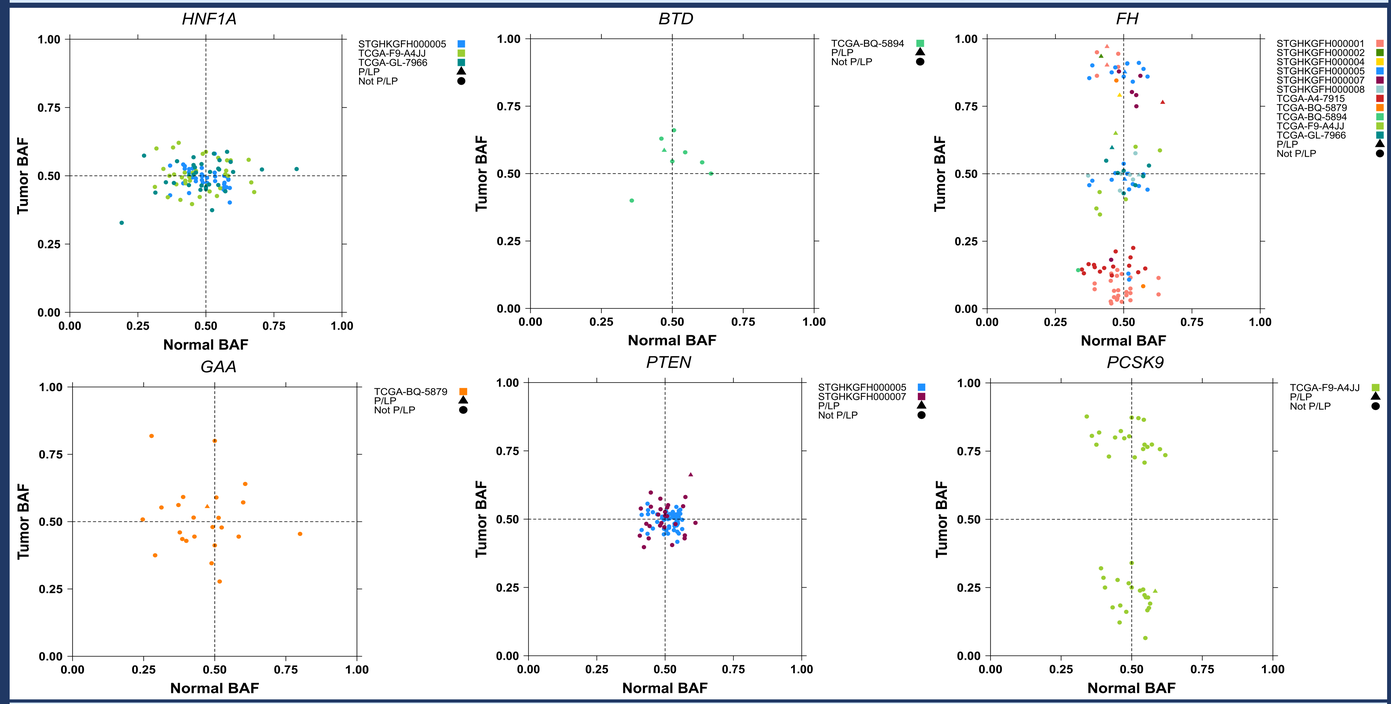


Figure 2: Tumor *vs.* Normal B-allele Frequency By Patient

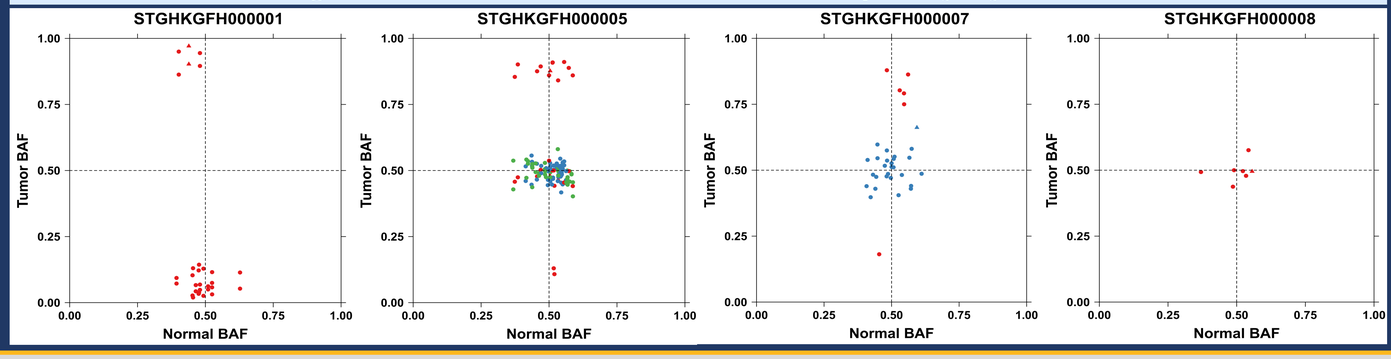
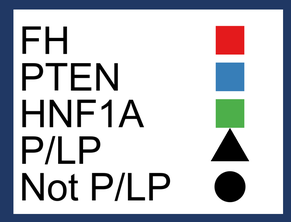


Figure 1 & 2: B-allele frequencies in paired tumor and normal samples from patients with FH-RCC. Alterations are grouped by Driver genes (**1**) and patient (**2**). Pathogenic / Likely pathogenic (P/LP) samples are highlighted in both figures. Pathogenicity was labeled in accordance with CLIN Var.



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