Lynch syndrome is a hereditary cancer syndrome that can lead to the development of many types of cancers, most commonly colorectal cancer [1]. Lynch syndrome can be caused by a mutation in MSH6, a protein involved in the DNA mismatch repair (MMR) pathway [2]. The gut microbiome is known to influence the development of colorectal cancer through many potential mechanisms [3]. It is unknown how the microbiome contributes to the development of colorectal cancer in individuals with Lynch syndrome.

My **primary goal** is to determine how the microbiome influences the development of colorectal cancer in Lynch syndrome caused by MSH6 mutation. I will use mice (*Mus Musculus)* as a model organism as their gut microbiome can be manipulated and they are well-studied as a cancer model [3]. My **hypothesis** is that MMR deficiency makes cells unable to repair DNA damage induced by some bacteria such as *Escherichia coli* and thus making them more susceptible to cancer development. My **long-term goal** is to discover if altering the microbiome of individuals with Lynch syndrome can decrease their chance of developing colorectal cancer.

**Aim 1: Determine microbiota related to Lynch syndrome colorectal cancer**

**Hypothesis:** I hypothesize that hereditary and sporadic MMR deficient colorectal cancers will be associated with different microbiota and Lynch syndrome colorectal cancer will not be associated with *Fusobacterium*.

**Approach:** I will sequence the microbiota obtained from tumor samples and normal adjacent tissue for patients with Lynch syndrome associated and sporadic MMR deficient colorectal cancer. I will then compare the abundance of species of bacteria between the two to determine microbial composition specifically associated with Lynch syndrome colorectal cancer.

**Rationale:** *Fusobacterium* is known to be associated with MMR deficient colorectal cancer and hypermethylation of the MMR protein MLH1 potentially due to the hydrogen sulfide it produces [4]. Hypermethylation of the MLH1 promoter is the main cause of sporadic MMR deficiency [5]. Given this, sporadic and Lynch syndrome MMR deficiency may be associated with different microbiomes.

**References:**

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