The microenvironment within tumors is critical to neoplasia. Non-neoplastic cells provide nutrients and growth factors that sustain tumor growth and promote progression of the neoplastic process. The complexity of these interactions is very difficult to study in vitro or in clinical settings. We have therefore been using a mouse model of intestinal neoplasia to better understand the neoplastic microenvironment in this organ system.

**APCMMin Mouse (Min)**

- Substitution mutation in murine Apc gene truncates protein at 850 amino acids (wt = 2843 aa)
- Fully penetrant autosomal dominant trait
- Homozygous embryonic lethal
- Heterozygous mice spontaneously develop multiple intestinal adenomas predominantly in the small intestine following spontaneous loss of the wild-type Apc allele (LOH)

**Modifier genes include**

- Loss of Apo product is only known mutation driving tumorigenesis
- Modifier genes include Mom-1 (AKR strain) and Mom-2

**Mucosal Mast Cells, TH2 Responses, & Nematode Infections**

Min mouse tumors frequently contain a unique cell type not present in the adjacent non-neoplastic mucosa. We’ve identified these cells as mucosal mast cells (MMC) based on immunohistochemical (IHC), histochemical and ultrastructural (EM) characteristics. In H&E stained sections these MMC resemble “globular leukocytes”.

MMC only appear in the context of TH2 immune responses and have been most extensively studied in intestinal nematode infections where they have been associated with expulsion of parasites. Key factors in this response include:

- IL-4 and/or IL-13
- chymase, mouse mast cell protease-1

Expression of some TH2 cytokines is in fact upregulated in Min mouse tumors compared to the adjacent normal intestine.

MMC may be found in small intestinal tumors from:

- Min mice
- Min x AKR mice carrying the dominant modifier allele Mom-1
- APCMin mice, including invasive tumors
- Unrelated mouse strains (spontaneous carcinoma)

Not all small intestinal tumors in Min mice contain MMC and they are not present in Min colorectal polyps.

MMC infiltrates do not appear to be related to affects of select pharmaceutical and dietary factors on tumorigenesis.

PGE2-receptor agonist treatment may increase the number of intratumoral MMC, but this is not associated with a significant impact on tumor growth.

**Relation to Tumorigenesis and Treatment Effects**

MMC may be found in small intestinal tumors from:

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**Conclusions**

It remains to be determined if this TH2 signaling pathway is important in mucosal mast cell infiltration in tumors, contributes to Min tumorigenesis, or is a target of various treatments or environmental factors that affect tumorigenesis in this model.

**Select References**