Pro-inflammatory Oncogenic Driver

Definition: A *pro-inflammatory oncogenic driver* is a genetic or molecular alteration that simultaneously promotes **malignant transformation** (oncogenesis) and **chronic inflammation**, fostering tumor development and progression.

Key Features

- Activates inflammatory signaling pathways (e.g., NF-κB, STAT3).
- Promotes cell proliferation, survival, and immune evasion.
- Shapes the tumor microenvironment to support angiogenesis and metastasis.
- Creates a positive feedback loop between inflammation and tumor growth.

Common Examples

Driver / Pathway	Role in Inflammation and Cancer
Mutated KRAS	Activates MAPK and NF-κB → increases pro-inflammatory cytokines.
MYC overexpression	Regulates inflammatory and metabolic genes in the tumor environment.
Constitutive NF-κB	Drives chronic inflammation and survival gene expression.
Activated STAT3	Induces IL-6, VEGF, and other oncogenic inflammatory mediators.
TP53 loss	Impairs immune surveillance → unresolved inflammation.
COX-2 overexpression	Elevates prostaglandins → enhances inflammation and tumor growth.

Clinical Relevance

- **Therapeutic Targeting:** These drivers are candidates for combined oncologic and anti-inflammatory therapies.
- **Biomarkers:** Their dual role makes them valuable prognostic or predictive biomarkers.
- **Immunotherapy Modulation:** Targeting these pathways may enhance immune responses against tumors.

References

- Greten, F.R., Grivennikov, S.I. (2019). Inflammation and Cancer: Triggers, Mechanisms, and Consequences. *Immunity*.
- Mantovani, A., et al. (2008). Cancer-related inflammation. *Nature*.