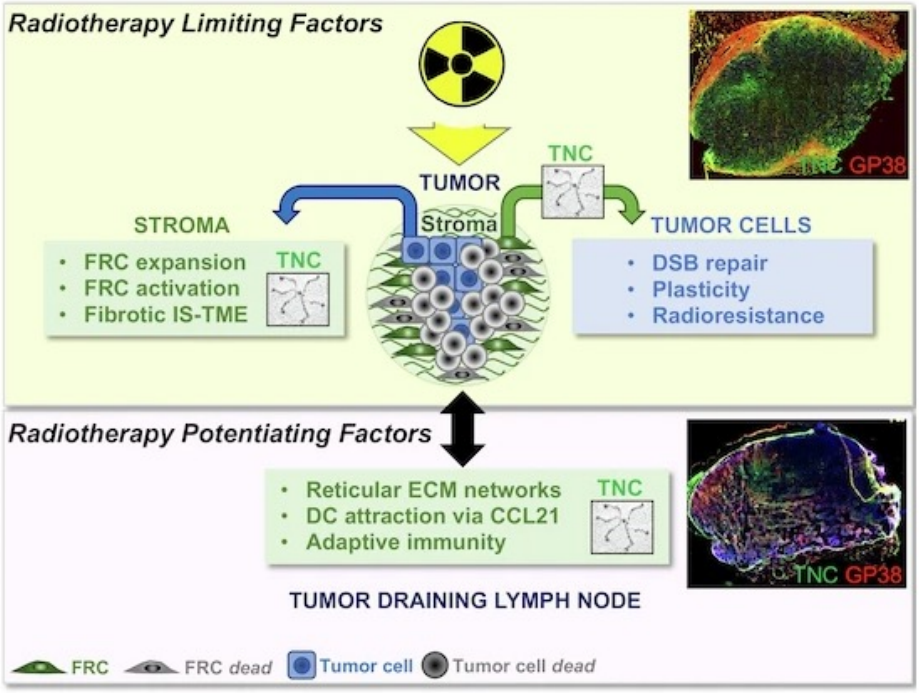
Loustau T et al., ***EMBO Mol Med*** DOI 10.1038/s44321-026-00406-8.

Synopsis



Radiotherapy lowers tumor burden but also induces tenascin-C (TNC), promoting immunosuppression and radioresistance; unlike in radiosensitive tumor draining lymph nodes, TNC-positive reticular fibroblasts promote tumor radioresistance, enabling radiosensitization by a TNC targeting MAREMO peptide.

- In HNSCC, fibroblast reticular cell (FRC) abundance is increased after radiotherapy through tenascin-C (TNC) dependent mechanisms.
- TNC is shown to determine distinct FRC phenotypes in the tumor microenvironment and tumor draining lymph nodes.
- TNC-dependent FRCs are demonstrated to promote tumor cell DNA double-strand break repair, plasticity and radioresistance.
- Radio-induced plasticity and tumor cell survival are shown to be reduced by TNC targeting with the MAREMO peptide.
- High intratumoral abundance of TNC-expressing FRCs is associated with inferior overall survival in HNSCC patients.