세미나 초록

성명	최진욱
소속	*광주과학기술원 생명과학과*
발표 주제	**Inflammation and stem cell plasticity in lung tissue generation and diseases**
발표 내용	Dysregulated interaction between stem cells and their niche represent the critical initiating event in pathologic transformation. Here, we map the spatiotemporal remodelling of tumour ecosystems, revealing how early alterations shape niche diversity to facilitate tumour development. By leveraging *in vivo* lineage tracing, single-cell transcriptomics, and *in vitro* organoid co-cultures, we identify the Amphiregulin (AREG)-EGFR axis as the primary driver of this process. Regenerative states of alveolar type II (AT2) cells harbouring $Kras^{G12D}$-mutation secret AREG to reprogramme fibrotic niche of adjacent alveolar fibroblasts through a regenerative programme. These reprogrammed fibroblasts subsequently remodel the immune microenvironment by reprogramming alveolar macrophage (AM) expansion to promote inflammation, while simultaneously supporting transition of tumour cell states. These interactions establish a self-reinforcing circuit leading to the distribution of distinct functional niches for early tumour development. Notably, genetic and pharmacological disruption of this AREG-EGFR axis prevents both niche cell reprogramming and tumour expansion. We confirm these interactions in early-stage human lung adenocarcinoma patients. Our human lung organoids with inducible *KRASG12D*-mutant gene demonstrate that oncogene activation drives fibrotic niche formation, suggesting a therapeutic strategy targeting tumour ecosystems at early stage, preventing establishment of treatment-resistant disease.