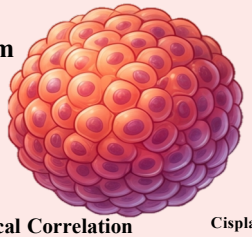
## HYPER-PROLIFERATIVE SPHERIODS

(HRPS)



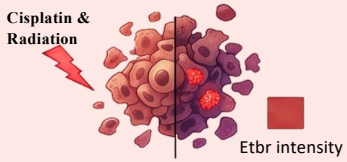

**HRPS Signature**

NDRG1
CA9
CCL20
FAM162A
STC2
TMEM123

**Clinical Correlation**



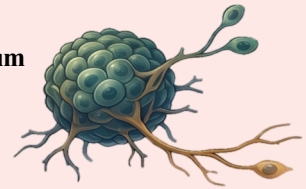

**Patient-derived HRPS shows predominance in Early stage tumors**

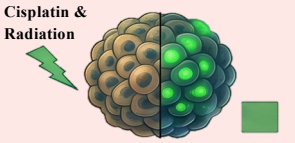



**Sensitive**

## HYPO-PROLIFERATIVE SPHERIODS

(HOPS)




**Resistant**

**Clinical Correlation**




**Patient-derived HOPS shows predominance in Late stage tumors**

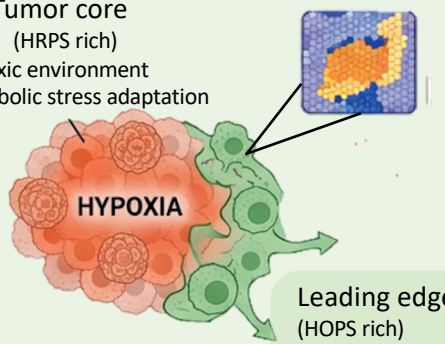
**HOPS Signature**

DSG3
DSC2
CSTB
S100A6
POLR2J3
FTH1

## SPATIAL COMPARTMENTALISATION

Tumor core
(HRPS rich)

- Hypoxic environment
- Metabolic stress adaptation

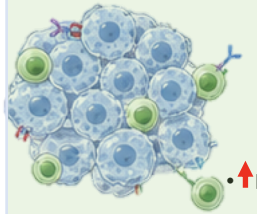



Leading edge
(HOPS rich)

- ECM remodelling
- Invasive

## IMMUNOLOGICAL EXCLUSION

**High HRPS**



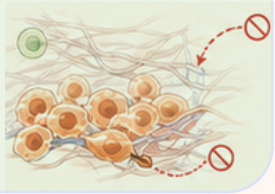
**Hot tumor**

(Moderate immune infilteration)
Immune checkpoints Expression

**High HOPS**

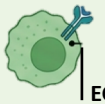
**Cold tumor**

(Low immune infilteration)
Immune checkpoints Expression



## TARGETABLE VULNERABILITY

**HOPS**




Active Invasive Program
**EGFR Dependent**

**Drug sensitivity**




**HRPS**



Metabolic Dependence



High HOPS/
High HRPS → **POOR PROGNOSIS**
"IMMUNE-COLD"
Resistant to Immunotherapy
Sensitive to EGFRi

Low HOPS/
High HRPS → **BETTER PROGNOSIS**
"IMMUNE-HOT"
Sensitive to Immunotherapy

**Understanding Sub clonal heterogeneity Enables Precision Medicine and Targeted therapies.**