Technology from Kyoto University

# A Plasma Biomarker for Hypoxic Fraction in Solid Tumors

We are looking to out-license the technology for its commercialization.

## *Plasma SPINK1 levels are correlated with the volume of hypoxic fractions in malignant solid tumors.*

### ◆ Background

Hypoxic regions (regions with a decreased partial pressure of oxygen) in malignant solid tumors are a key environmental factor that enhances the resistance of cancer cells to radiotherapy and anticancer chemotherapy. Lower oxygen levels in tumors are also known to be associated with advanced malignancy. Therefore, assessing the volume of hypoxic regions and the degree of hypoxia in tumor tissues is critical not only for monitoring their pathological conditions and predicting therapeutic effects on them but also for developing a novel strategy for personalized cancer therapy. However, currently available methods to detect hypoxia are invasive such as PET imaging and IHC on biopsy.

### ◆ Description

Researchers at Kyoto University found that the expression and secretion of SPINK1 are immediately increased upon severe but not mild hypoxia and returned to their basal levels after reoxygenation (**Fig. 1**). In addition, they found a positive correlation between the levels of SPINK1 in plasma and the volume of hypoxia in the tumors (**Fig. 2**). Furthermore, they confirmed that SPINK1 increases the radioresistance of cancer cells (**Fig. 3**). These findings suggest that SPINK1 can be used as a “minimally invasive plasma biomarker" to monitor "tumor hypoxia" and "tumor malignancy".

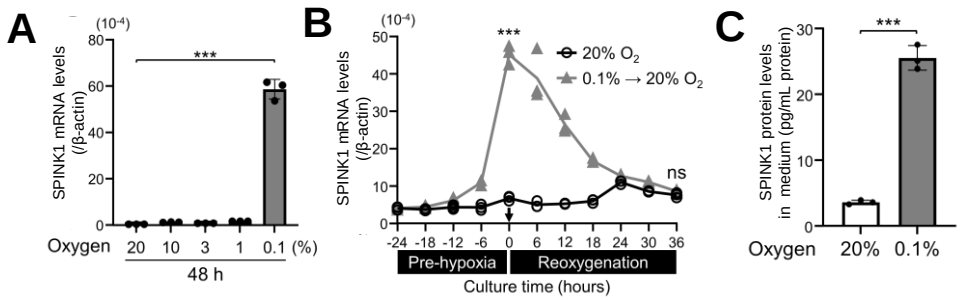


**Fig. 1** Cancer cells stimulated by hypoxia express and secrete SPINK1

A human cervical carcinoma cell line, HeLa cells, expressed (A, B) and secreted (C) SPINK1 upon hypoxic stimulus. The hypoxia-dependent expression returned to the basal levels upon reoxygenation treatment (B).

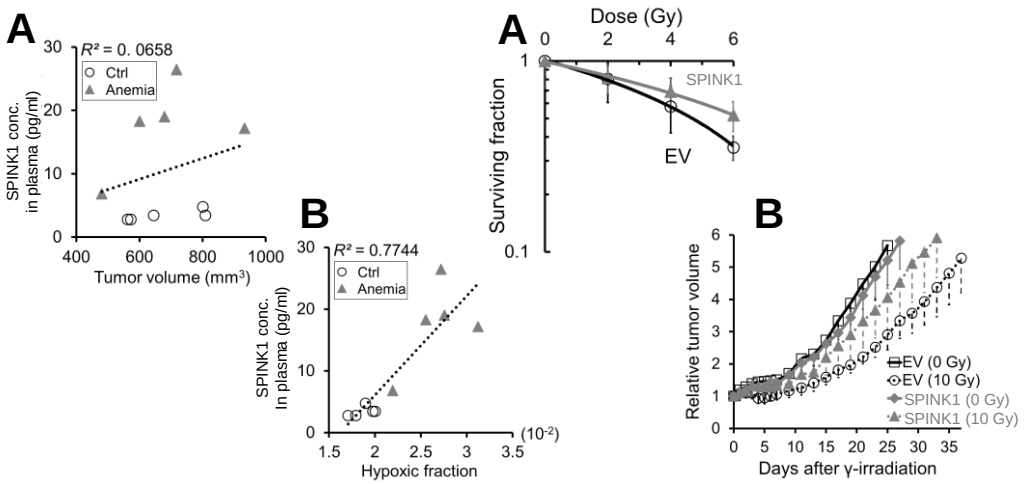


**Fig. 2** The volume of hypoxic regions in malignant solid tumors is correlated with the concentration of SPINK1 in plasma.

Tumor xenografts with various hypoxic fraction were produced by administrating a hemolytic agent (phenylhydrazine) into tumor-bearing mice with a HeLa xenograft. The concentration of SPINK1 in the plasma did not correlate with tumor volume (A, $R^2 = 0.0658$), but strongly correlated with the hypoxic fractions in tumor tissues which were monitored as the levels of endogenous hypoxia marker, CA9 (B, $R^2 = 0.7444$).

**Fig. 3** SPINK1 promotes the radioresistance of cancer cells.

(A) Colony formation assay confirmed that HeLa cells transfected with SPINK1-expressing vector acquired more radioresistance than those transfected with an empty vector (EV). (B). Tumor-bearing mice transplanted with the SPINK1-expressing HeLa cells were subjected to local treatment with gamma rays and subsequent tumor growth was measured. Overexpression of SPINK1 accelerated tumor regrowth after radiotherapy.

### ◆ Development Status

*Verified in vitro / in vivo:*

- Hypoxia-stimulated cancer cells express SPINK1 and secrete SPINK1 into the blood.
- The concentration of SPINK1 secreted into the plasma can be used as an indicator to monitor the hypoxic volumes in the tumor.
- Pancreatic cancer patients with higher plasma SPINK1 levels show lower survival rates.

### ◆ Publication

Suwa et al., JCI Insight (2021) https://doi.org/10.1172/jci.insight.148135.

### ◆ Application

- In vitro diagnostic reagents
- Reagents
- Drug discovery (therapeutic targets)

### ◆ Offer

- License
- Option for license

### ◆ Contact

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