SELECTED OPPORTUNITY IN ONCOLOGY

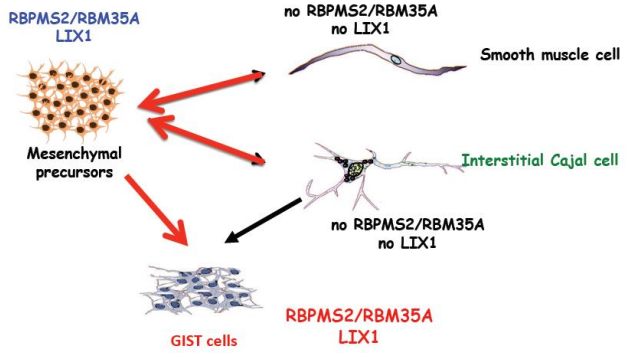
METHODS FOR THE DIAGNOSIS AND TREATMENT OF GASTROINTESTINAL STROMAL TUMORS (BIO13315)

METHODS FOR THE DIAGNOSIS AND TREATMENT OF GASTROINTESTINAL STROMAL TUMORS (BIO13315)

Product factsheet

PoC *in vivo*

- **Target:**
  - Limb Expression 1 (*LIX-1,* BIO 13315)
- **Product:**
  - Antisens oligonucleotide (in development)
  - Small molecule (to be developed)
- **Application:**
  - Gastrointestinal stromal tumors (GISTs)

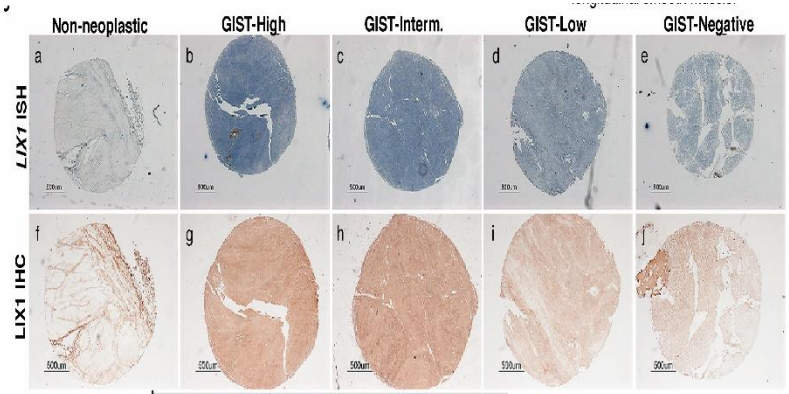


- **Rational / POC:**
  - GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract
  - *LIX1* is a unique marker of stomach mesenchymal progenitors, its expression is strong and highly dynamic
  - *LIX1* positively regulates cell proliferation and SMC determination
  - Sustained LIX1 expression resulted in an expanded determined SMC domain, SMC differentiation, the later step of SMC development, was hindered, demonstrating the requirement for a tight regulation of LIX1 expression during stomach mesenchyme development
  - *LIX1* is expressed in GISTs, highlighting cell immaturity within GISTs, and high *LIX1* expression is associated with poor patient prognosis
- **Patent and publication:**
  - McKey J, Martire D, de Santa Barbara P, Faure S. *LIX1 regulates YAP1 activity and controls the proliferation and differentiation of stomach mesenchymal progenitors*. BMC Biol. 2016 Apr 28;14:34. doi: 10.1186/s12915-016-0257-2.
  - WO2017137545: METHODS FOR THE DIAGNOSIS AND TREATMENT OF GASTROINTESTINAL STROMAL TUMORS

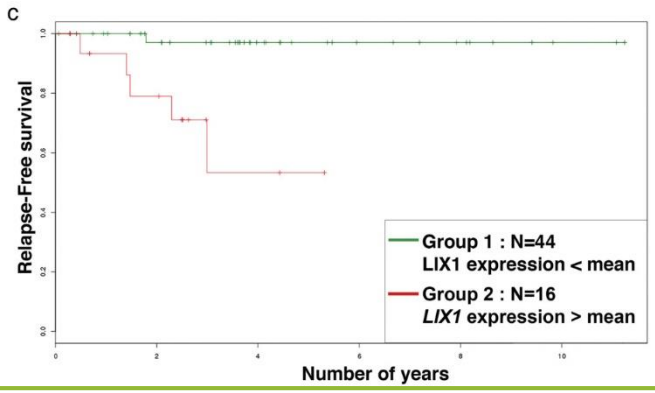
METHODS FOR THE DIAGNOSIS AND TREATMENT OF GASTROINTESTINAL STROMAL TUMORS (BIO13315)

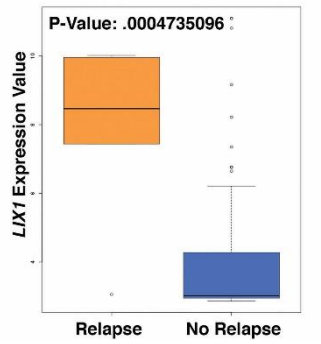
Proof of concept

LIX1 is highly expressed in GISTs and its expression is associated with unfavorable prognosis



Expression	High	Intermediate	Low	No
LIX1 mRNA	7/21 (33%)	9/21 (43%)	4/21 (19%)	1/21 (5%)
LIX1 protein	4/21 (19%)	4/21 (19%)	7/21 (33%)	6/21 (28%)



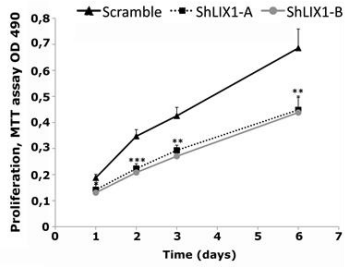


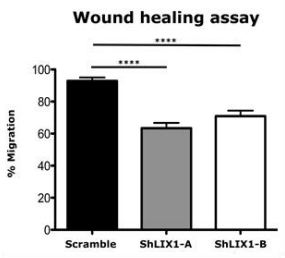
METHODS FOR THE DIAGNOSIS AND TREATMENT OF GASTROINTESTINAL STROMAL TUMORS (BIO13315)

Proof of concept

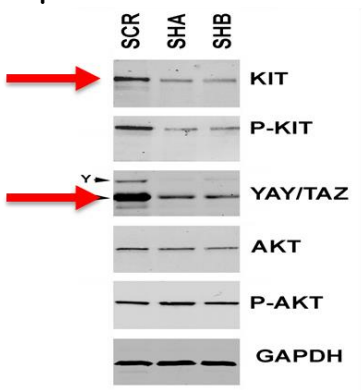
Inhibition of LIX1 in GISTs and resistance to Imatinib

- LIX1 silencing decreases cell proliferation and migration

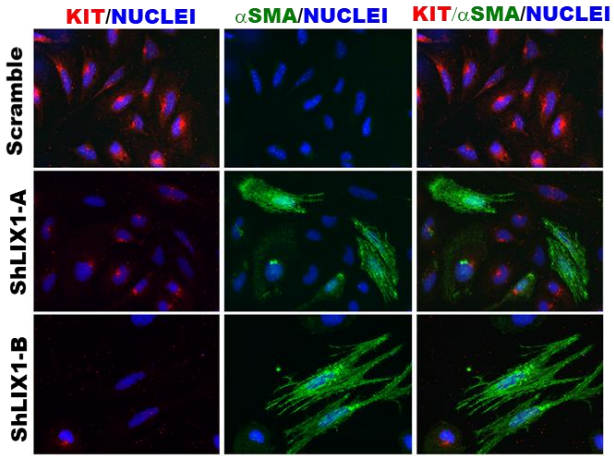




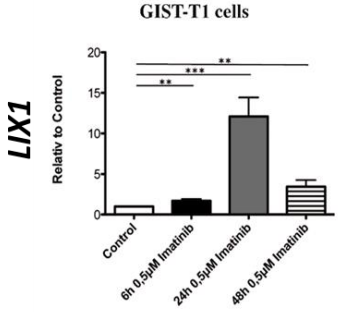
- LIX1 silencing decreases YAP/TAZ and KIT expression

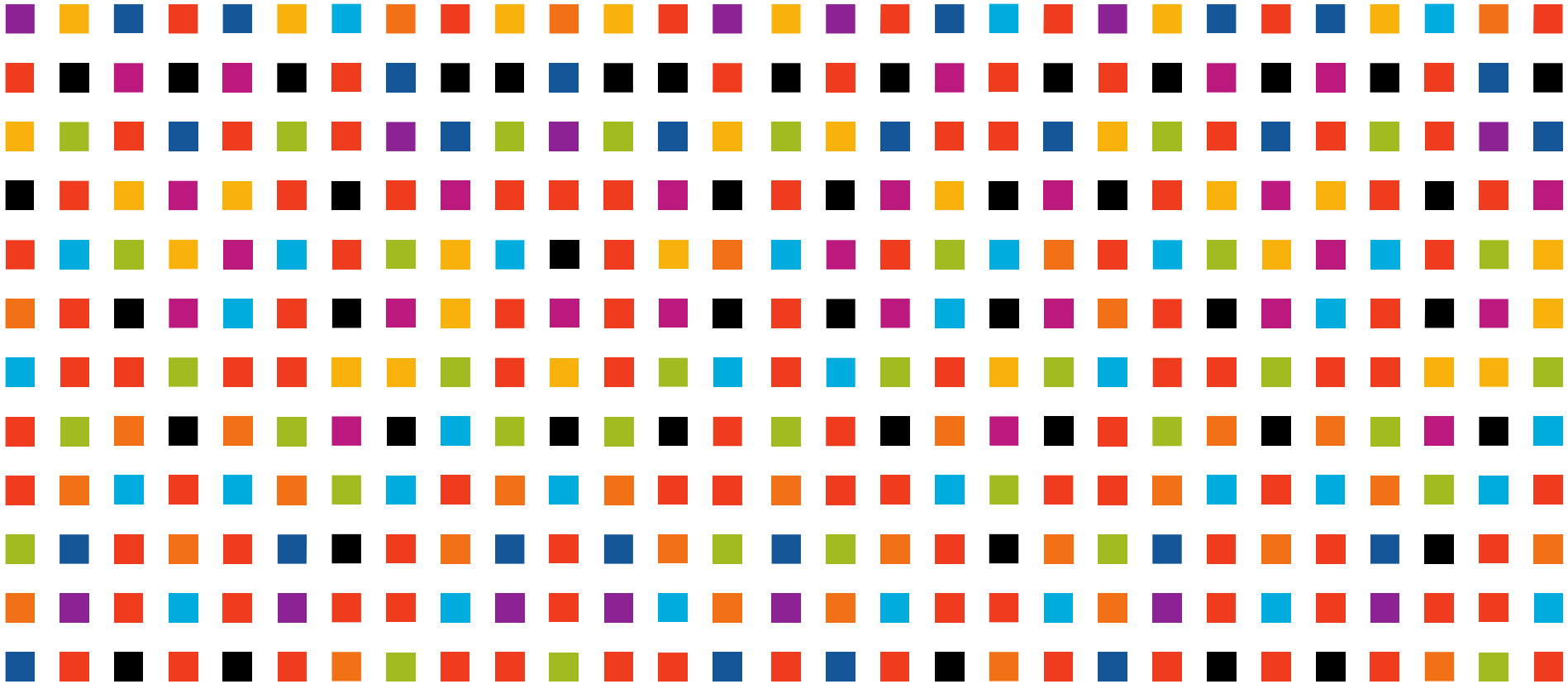


- LIX1 silencing increases SMC determined markers



- Imatininb treatment induces LIX1 expression





ANNE.COCHI@INSERM-TRANSFERT.FR