

ORIGINAL ARTICLE

Biological and targeting differences between the rare KRAS A146T and canonical KRAS mutants in gastric cancer models.

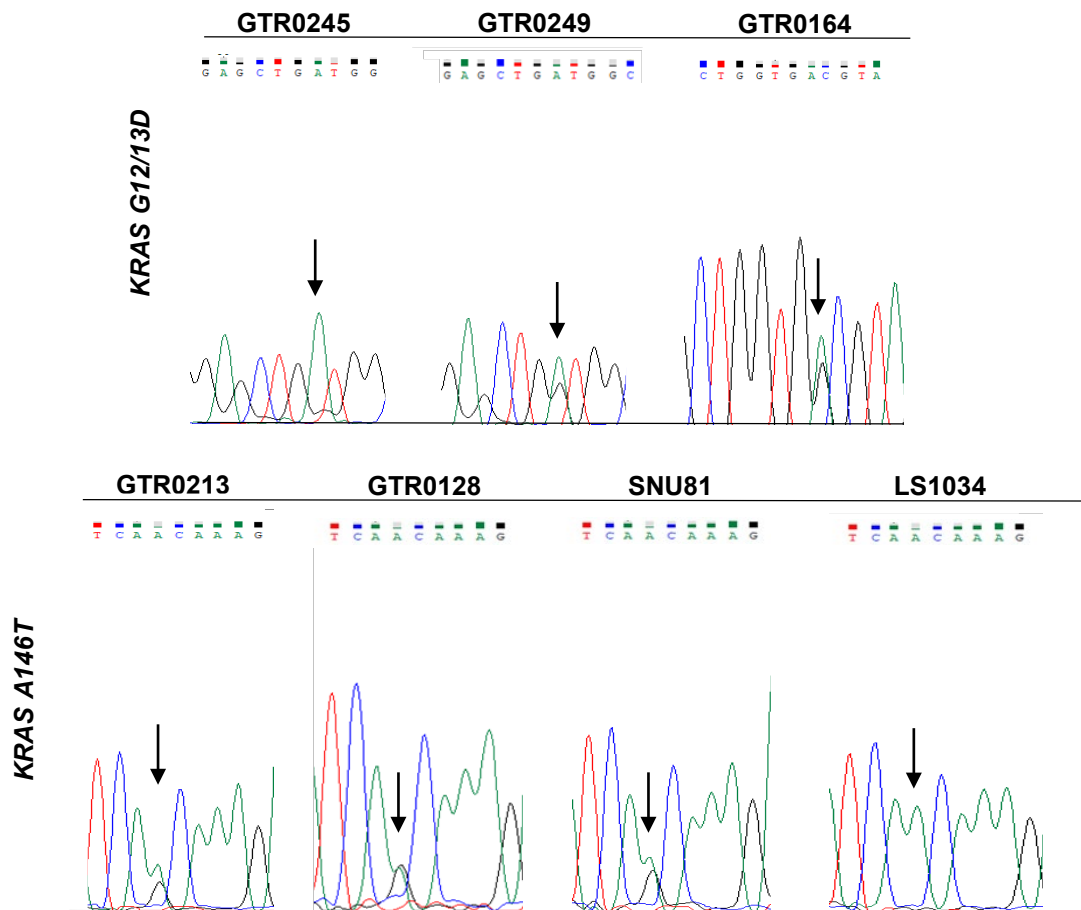
Elisabetta Puliga^{1,2*} Chiara De Bellis^{1,2}, Sandra Vietti Michelina³, Tania Capeloa^{1,2}, Cristina Migliore^{1,2}, Claudia Orrù^{1,2}, Gian Luca Baiocchi^{4,5}, Giovanni De Manzoni⁶, Filippo Pietrantonio⁷, Rossella Reddavid⁸, Uberto Fumagalli Romario⁹, Chiara Ambrogio³, Simona Corso^{1,2} and Silvia Giordano^{1,2}.

¹Department of Oncology, University of Torino, Candiolo, Italy. ²Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy. ³Department of Molecular Biotechnology and Health Sciences, Molecular Biotechnology Center, University of Torino, Via Nizza 52, 10126 Torino, Italy ⁴Department of Clinical and Experimental Sciences, University of Brescia, Italy; ⁵Department of Surgery “Santo Spirito Hospital”, ASL-AL; ⁶Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, Section of Surgery, University of Verona, Italy; ⁷Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; ⁸Department of Oncology, University of Torino, Orbassano, Italy; ⁹Digestive Surgery - European Institute of Oncology - IRCCS – Milan;

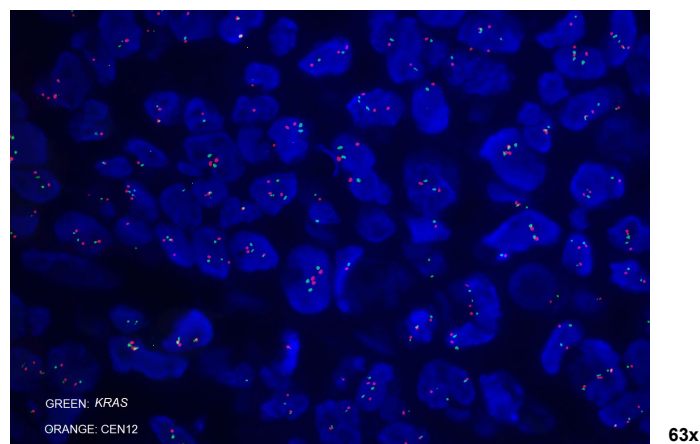
*Corresponding author: elisabetta.puliga@ircc.it, +39 011 993321

Supplementary Figure 1

a

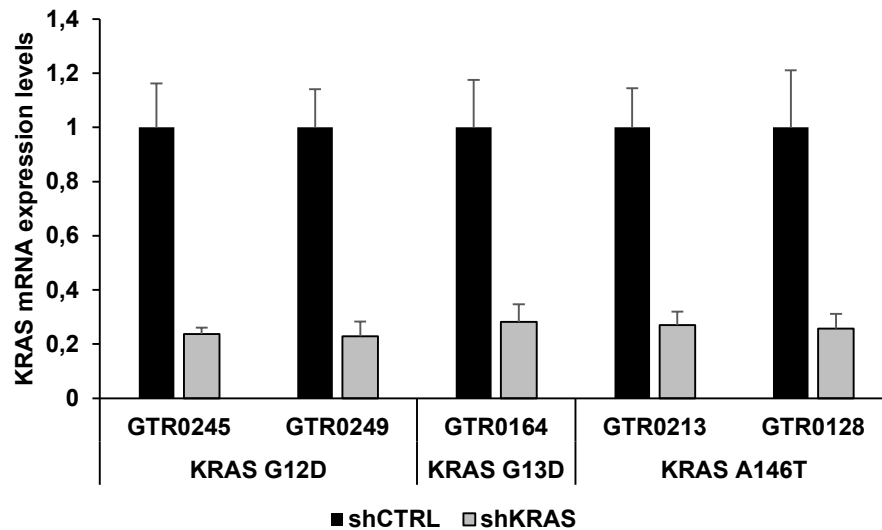


b



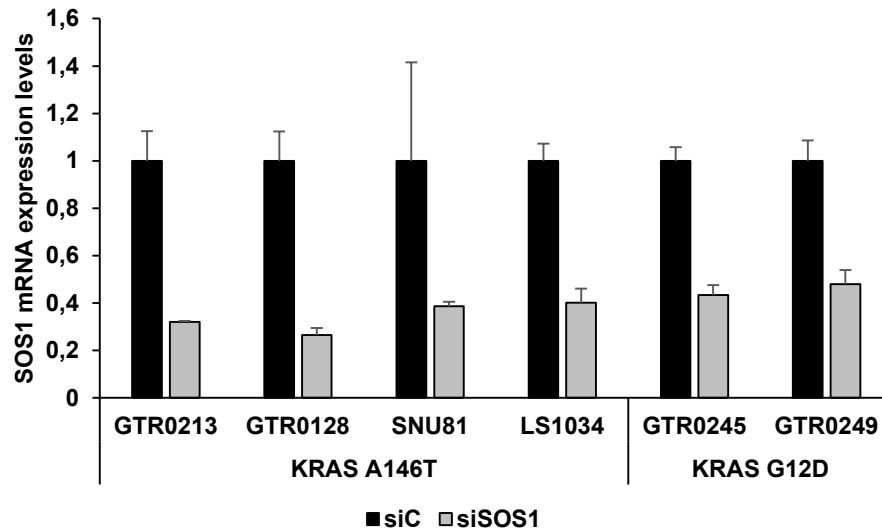
Supplementary Figure 1 *KRAS* gene mutations in Gastric Cancer PDX models used *in vitro* and *in vivo* experiments. (a) Electropherograms obtained by Sanger sequencing showing *KRAS* mutations in the different models. (b) *KRAS* fluorescence *in situ* hybridization for the GTR0245 PDX. *KRAS* (green) and CEN12 (red) signals (63x magnification).

Supplementary Figure 2



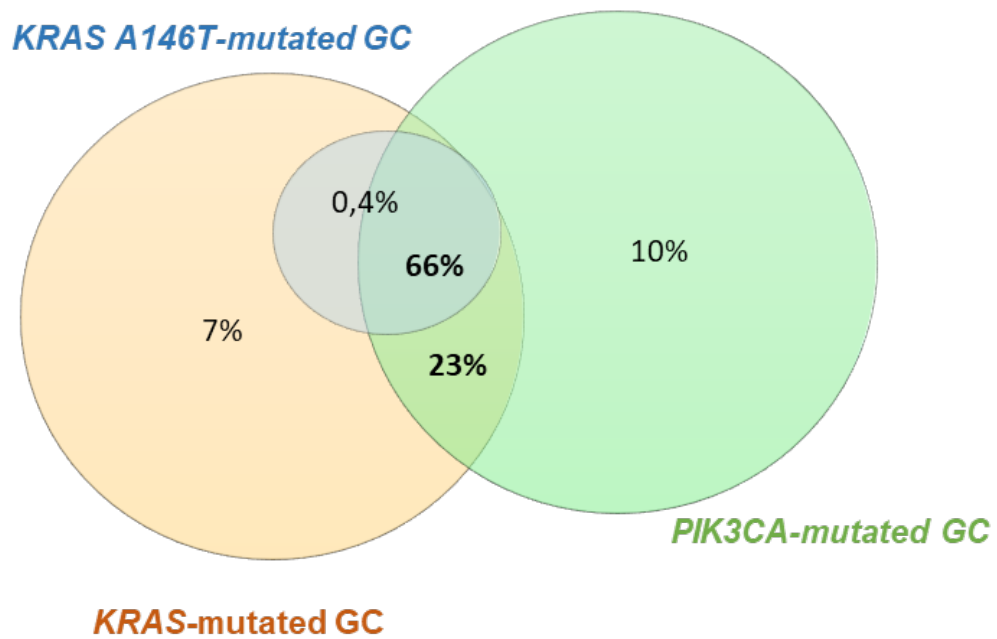
Supplementary Figure 2 Effectiveness of KRAS silencing. 48h after cell transduction with either control siRNA or KRAS siRNA, *KRAS* mRNA was quantified by qRT-PCR. The graph shows the percentage of expression in KRAS silenced cells vs controls.

Supplementary Figure 3



Supplementary Figure 3 Effectiveness of SOS1 silencing. The efficacy of *SOS1* silencing was demonstrated by measuring SOS1 mRNA levels by qRT-PCR 48h after transfection with either control siRNA or SOS1 siRNA.

Supplementary Figure 4



Supplementary Figure 4 Co-occurrence of *KRAS* and *PI3KCA* mutations in GC. Venn diagram showing the co-occurrence of canonical *KRAS*, *KRAS A146T* and *PI3KCA* mutations in a cohort of 777 gastric cancer patients. Five different gastric cancer databases were interrogated on cBioportal.