DBPR117:

A precision medicine (mAb) targeting RSPO3/Wnt signaling and PD-1 blockade efficacy

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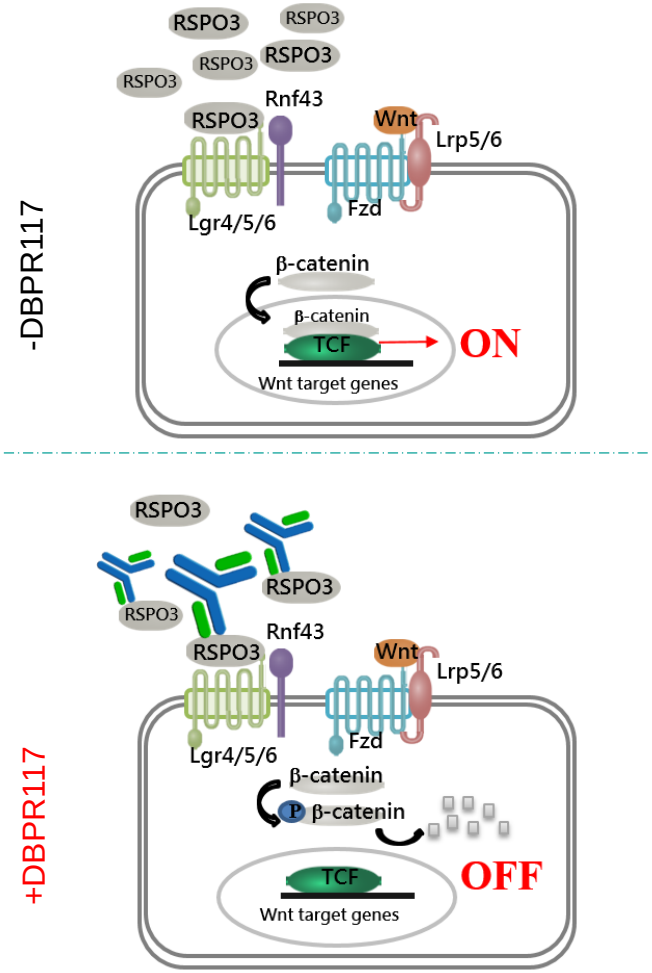
Anti-RSPO3 Antibody DBPR117 : Executive summary

Several lines of evidence supported that anti-RSPO3 antibody is effective in treating cancers with RSPO3 dysregulation.

- DBPR117, alone or in combination with other drugs, can be used to treat cancers with RSPO3-fusion / overexpression.
- DBPR117 in combination with anti-PD1 antibody would synergize to combat melanoma cancers in a B16F10 syngeneic murine models.
- DBPR117 can be used for diagnosis of RSPO3 levels using ELISA, IHC.
- DBPR117, when conjugated with an image probes, can be used to identify or trace RSPO3-overexpression cancers in animals.



RSPO3-dependent cancers with unmet medical needs

Market Niche I

CRC (mtKRAS)

Incidence : 50% of CRC
genotype : $KRAS^{G12C}$
$RSPO3^{high}$

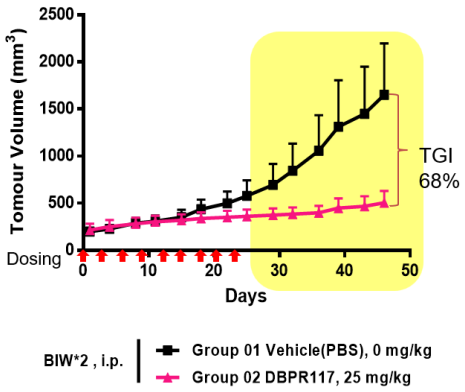
Treatment options	Response Rate	PFS	Resistance development
Trametinib	26%	8.7 mos	High

NSCLC (mtKRAS, wt EGFR)

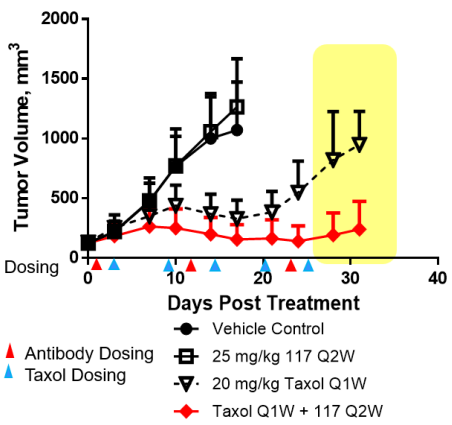
Incidence : 24 % of NSCLC
genotype : $KRAS^{G12C}$
$RSPO3^{high}$

Treatment options	Response Rate	PFS	Resistance development
Trametinib	12%	12 wks	
Docetaxel	12%	11 wks	NA

CR3150 PDX model
(PTPRKe1-RSPO3e2 , $KRAS^{G12V}$)

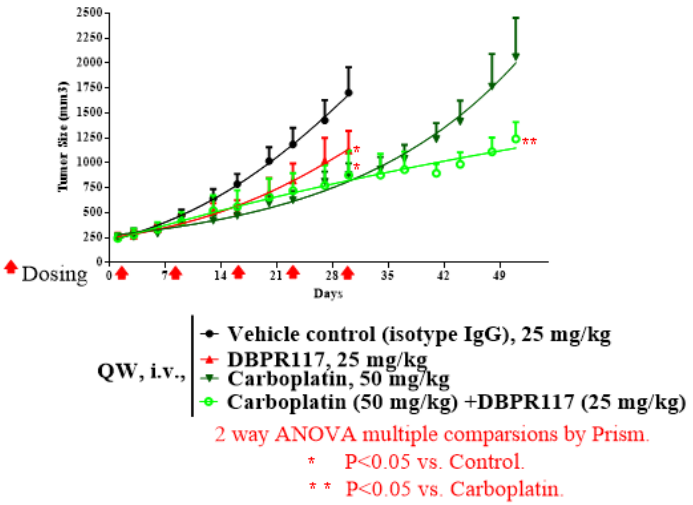


SNU-1411 CDX model
(PTPRKe13-RSPO3e2, $KRAS^{G12C}$)



Lung cancer CDX model NCI-H2030 cells
RSPO3 Overexpression

Genotype: $TP53^{G262V}$, $KRAS^{G12C}$, $RSPO3^{high}$, $STK11^{E317}$

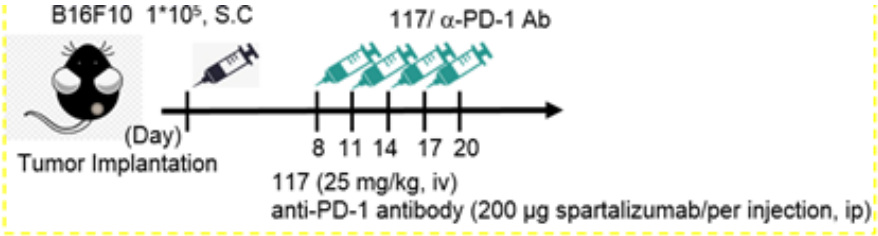


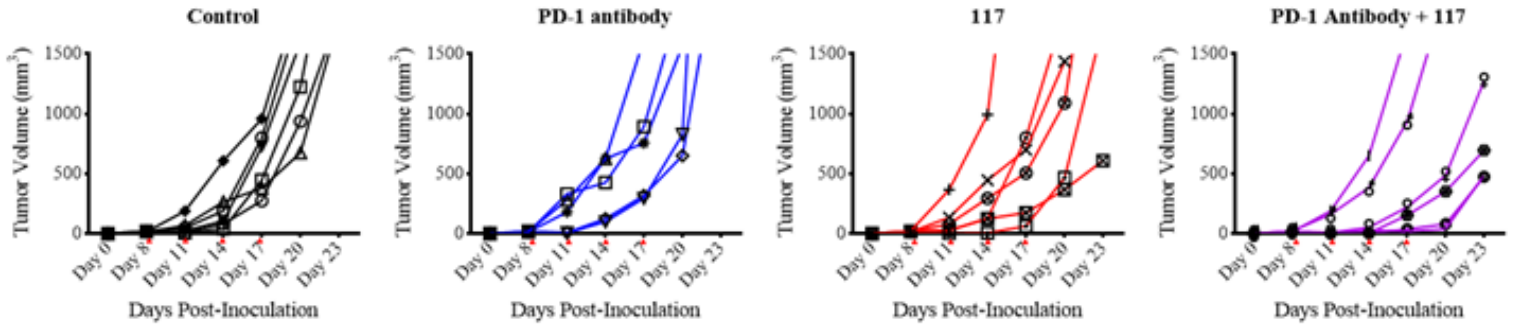
2 way ANOVA multiple comparsions by Prism.
* P<0.05 vs. Control.
** P<0.05 vs. Carboplatin.

Wnt/β-catenin pathway and immune activation – clinical correlation

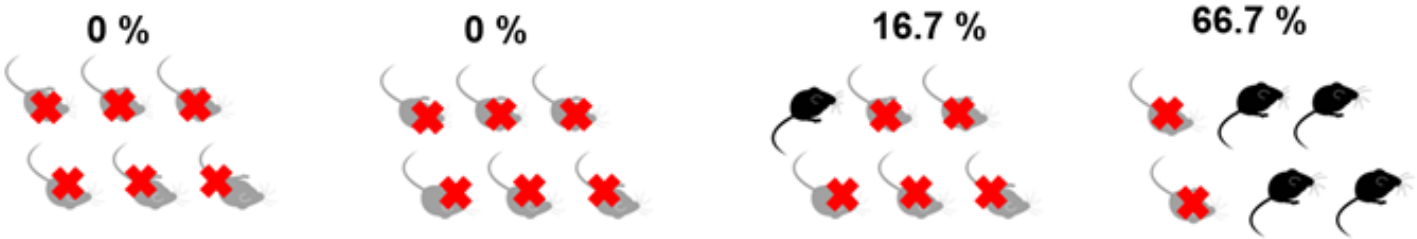
Market Niche II

Interactions between RSPO/Wnt and PD-1/PD-L1 pathway: Implications for treatment of malignant melanoma.





Overall Survival Rate on day 23



DBPR117 can turn the cold B16-derived tumors hot (no longer inert to PD1 blockade).

Major Advantages and Differentiation of DBPR117

- DBPR117 is capable of binding specifically to the human RSPO3 with novel amino acid sequences in the complementary determining regions (CDRs).

- DBPR117 may target a novel epitope of the RSPO3 Furin region (56-75 residues) to neutralize RSPO-WNT pathway.

- Compared to OncoMed's Rosmantuzumab, DBPR117 has different binding and dissociation mode and DBPR117 was superior to Rosmantuzumab in the NCI-H2030 Lung cancer CDX model.

- Targeting RSPO3 as a secreted angiogenic factor may provide novel opportunities for DBPR117 (Park *et al*., J. Biol. Chem., 2018)