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An APC activator (IMP321 or LAG-3Ig) combined with anti-PD-1 blockade

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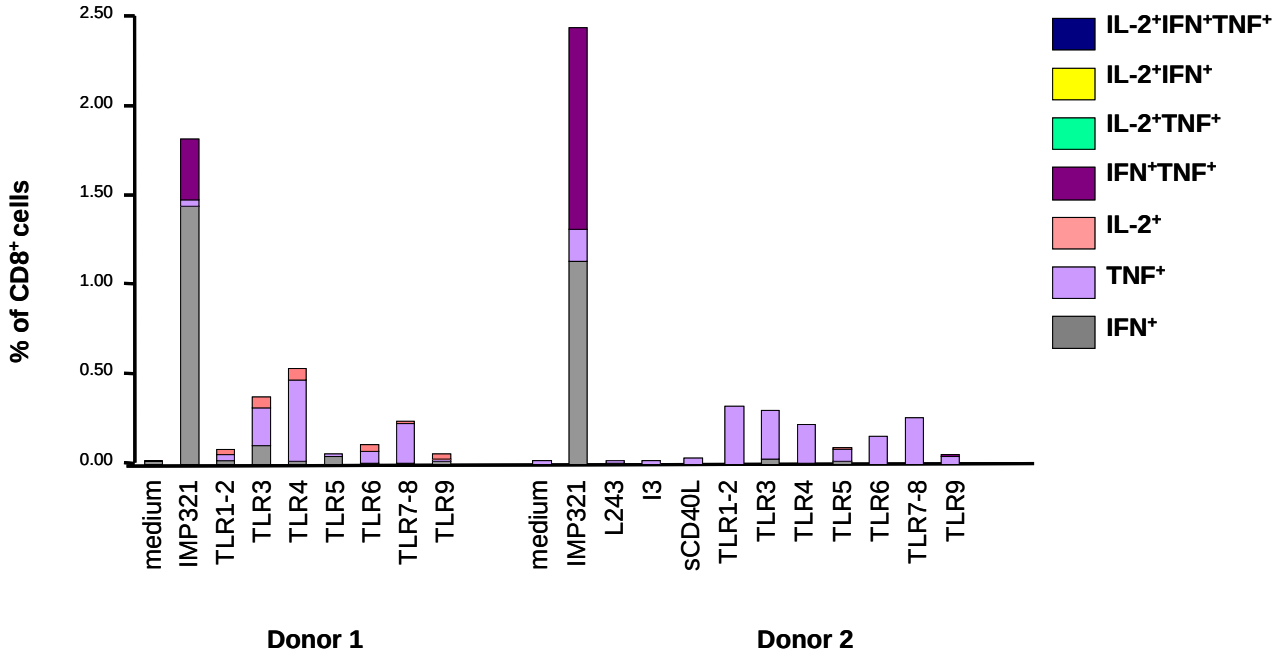
Three groups of patients responding to anti-PD-1 (IFN-γ signature)

- A- Inflamed responders – respond to anti-PD-1
- B- Inflamed non-responders (some infiltrates in the tumor margins but no response)
- C- Non inflamed. “Cold tumor” with no response

- Optimal checkpoint combos will target groups B and C and help them:
  - Promote cross presentation of tumor antigens
  - Induce T cell recruitment into tumor microenvironment

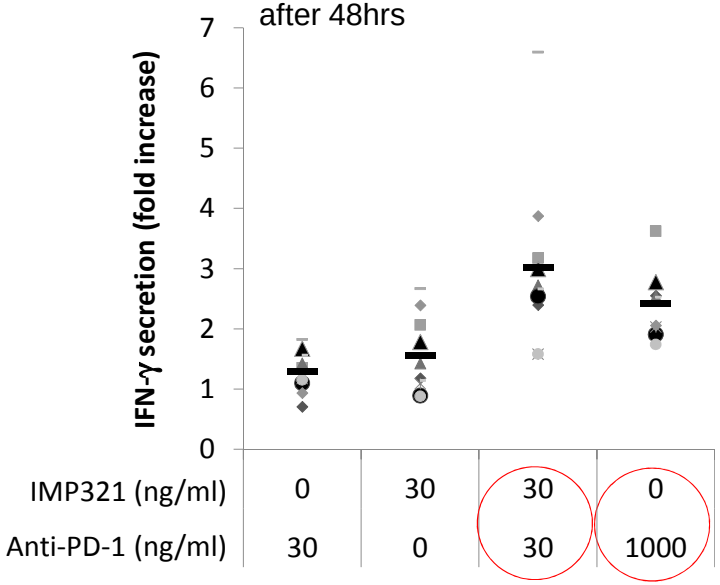
IMP321 induces a better Tc1 differentiation than sCD40L or TLR agonists

- **Human blood lymphocytes are analyzed in a 16 hr *ex vivo* assay**
- **Intracellular staining of CD8 T cells**
  - **Only IMP321 induces IFN$^+$ CD8 T cell responses**
  - **TLR agonists but not IMP321 induce IL-10 production which suppresses Tc1 differentiation**

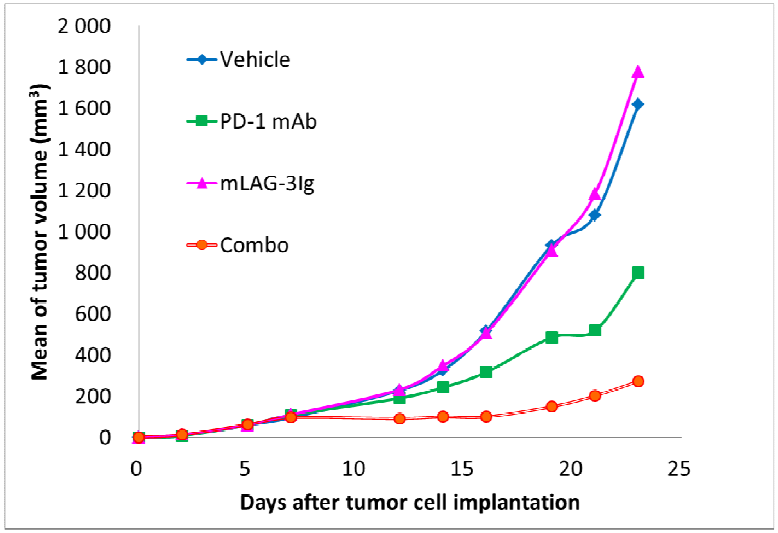


In vitro and *in vivo* preclinical data supporting the combination

CMV-stimulated PBMCs from 10 healthy donors after 48hrs



Anti-PD-1 (10 mg/kg) + mLAG-3Ig (1 mg/kg)
In a subcutaneous CT26wt colon cancer model



TACTI-mel: Two ACTive Immunotherapeutics in melanoma

Phase I study in immuno-immuno combination in unresectable or metastatic melanoma in Australia

up to 24 patients, 3 cohorts, max. 8 patients each → IMP321 + anti-PD-1 (Keytruda®) → Multicenter, open label, dose escalation → Safety and tolerability

First patient in May 2016

Design	Phase I, multi-centre, open-label, dose escalation
Primary Objective	Safety, tolerability and recommended dose finding for phase II with pembrolizumab + IMP321 in unresectable or metastic melanoma
Other Objectives	Pharmakokinetic and pharmakodynamic of IMP321, objective response rate, time to next treatment, progress-free survival
Patient Population	Patients with asymptomatic or suboptimal response after three cycles of pembrolizumab
Treatment	Up to 24 patients 3 cohorts: 1/6/30 mg IMP321; s.c. q2w + pembrolizumab; starting with the 5th cycle of pembrolizumab

Status report

- 6 clinical sites are approved and all are activated
- Dose escalation decision of the interim data of the first cohort is expected at the end of this year