Highlights of Basic Science
Basic Science Topics

- GS1_03. Crosstalk between osteoblasts and breast cancer cells alters breast cancer proliferation through multiple mechanisms
- GS3_06. Dynamics of breast cancer relapse reveal molecularly defined late recurring ER-positive subgroups: Results from the METABRIC study
- GS3_07. Clinical utility of circulating tumor cell count as a tool to choose between first line hormone therapy and chemotherapy for ER+ HER2- metastatic breast cancer: Results of the phase III STIC CTC trial.
- GS1_05. Apobec3 induced mutagenesis sensitizes triple negative breast cancer to immunotherapy by activating B-cells and CD4+ T-cells
Bussard et al. Crosstalk between osteoblasts and breast cancer cells alters breast cancer proliferation through multiple mechanisms  
Abs. GS1-03
Crosstalk between osteoblasts & breast cancer cells alters breast cancer proliferation

Objective: Analyze mechanisms of crosstalk between osteoblasts & breast cancer cells that alter breast cancer cell proliferation

- A subpopulation of osteoblasts are altered in the tumor niche in both murine and human samples
- Educated osteoblasts express different proteins than naïve osteoblasts
- Exposure to EO conditioned medium or exosomes reduces triple negative and ER+ breast cancer proliferation \textit{in vitro}
- Co-culture with EOs increases p21 expression in triple negative and ER+ breast cancer cells EOs have tumor-inhibitory properties
Dynamics of breast cancer relapse reveal molecularly defined late recurring ER-positive subgroups: Results from the METABRIC study

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Dynamics of breast cancer relapse: Results from the METABRIC study

- A subset of women with early stage ER+ BC have a persistent risk of recurrence and death up to 20 years post diagnosis
- 3240 breast cancer patients derived from 5 tumor banks in the UK and Canada diagnosed between 1977-2005
- Long term clinical follow-up; median 14 years
- Risk of relapse and timing of relapses differ across the major breast cancer subgroups
- Identify four high-risk subgroups that account for 26% of ER+ tumors and the majority of late relapses; each with characteristic ‘driver’ alterations
- Integrative subtypes improve the prediction of late relapse compared with clinical covariates
- Future direction - opportunities for improved patient stratification and biomarker-driven clinical trials for the quarter of ER-positive women with persistent risk of recurrence
Bidard et al. Clinical utility of circulating tumor cell count as a tool to choose between first line hormone therapy and chemotherapy for ER+ HER2- metastatic breast cancer: Results of the phase III STIC CTC trial Abs. GS3-07
Clinical utility Circulating Tumor Cells: Results of the phase III STIC CTC trial

- No predictive marker to choose between hormone therapy (HT) vs chemoT (CT) in metastatic BC
- HT is preferred in absence of endocrine resistance or visceral crisis
- Goal of this trial: to compare CTC-driven vs clinician's choice for 1st line therapy in HR+ metastatic BC
- Primary endpoint: progression free survival non-inferiority

Main inclusion criteria
- HR+ HER2- MBC
- No prior therapy for MBC
- Condition compatible with HT or CT
- PS 0-3
- Evaluate disease
- Informed consent

1:1 randomization  stratified on PS / center / disease-free interval

Clinician’s choice
CTC count: blinded

- HT (Clin_{low})
- CT (Clin_{high})

CTC count (CellSearch®) ?
Clinician’s choice: dismissed
- < 5 CTC /7.5mL  \rightarrow  HT (CTC_{low})
- \geq 5 CTC /7.5mL  \rightarrow  CT (CTC_{high})

Trial opened from 02/2012 to 07/2016 in 17 centers
N= 778 pts randomized

Median follow-up: 30 months
N= 605 PFS events (78% maturity)
N= 230 OS events (30% maturity)
Clinical utility Circulating Tumor Cells: Results of the phase III STIC CTC trial

Conclusion: In patients with ≥5 CTC/7.5mL, chemotherapy is better than single agent endocrine therapy.
Hollern et al. Apobec3 induced mutagenesis sensitizes triple negative breast cancer to immunotherapy by activating B-cells and CD4+ T-cells Abs. GS1-05
Apobec3 induced mutagenesis sensitizes triple negative breast cancer to immunotherapy by activating B-cells and CD4+ T-cells

- TNBC mouse models will present variable responses to immune checkpoint inhibitors, and that by using sensitive and resistant mouse models we can identify biomarkers of response
- Increasing mutation load of TNBC mouse models sensitizes tumors to immune checkpoint therapy and increases immune cell infiltration.
- Created a RNA-seq dataset of 290 mouse mammary tumors from multiple GEM Models annotated for treatment &
Apobec3 induced mutagenesis sensitizes triple negative breast cancer to immunotherapy by activating B-cells and CD4+ T-cells

- Identified a B Cell/T Cell Co-cluster expression signature that predicts response to immune checkpoint therapy, neoadjuvant chemotherapy, and trastuzumab+paclitaxel
- Identified a functional role for B Cells in mediating a response to immune checkpoint inhibitors in GEM Models.