Welcome to SITC 2019 Industry Committee Symposium:

Novel Multi-Targeted Therapeutic Platforms

Program Organizers:

- ***Alessandra Cesano, MD PhD – ESSA Pharma Inc***
- ***Edward Cha, MD PhD – Genentech***
- ***Leena Gandhi, MD PhD – Eli Lilly***
- ***Israel Lowy, MD PhD – Regeneron***
- ***Salil Patel , PhD – Bristol-Myers Squibb***
- ***Eric Rubin, MD – Merck & Co. Inc.***

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A. Cesano Disclosures

- Chief Medical Officer ESSA Pharma Inc
- Clinical Consultant for Nanostring Inc, Refuge
- Scientific Advisory Board for Arch Oncology, Qognit

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Session 1: Basics of Multi-Targeted Therapeutic Platforms				
Faculty	2:05 – 2:15 p.m.	10	Overview of Different Platform Structures	Alessandra Cesano, MD, PhD – *ESSA Pharma Inc.*
Faculty	2:15 – 2:35 p.m.	20	Harnessing Cytokines for Anti-Tumor Immunity	Raphael Clynes, MD, PhD – Xencor, Inc.
Faculty	2:35 –2:55 p.m.	20	Multi-Targeted CAR T cells	Marcela V. Maus, MD, PhD – *Massachusetts General Hospital*
Faculty	2:55 – 3:15 p.m.	20	Making NK Cells Antigen Specific With Engagers	Jeffrey S. Miller, MD – *University of Minnesota*
	3:15 – 3:30 p.m.	15	Break	

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Compared with mono-target therapeutic the increased complexity associated with multi-targeting targeting can provide additional challenges during different stages of discovery and development

Panel Discussion	3:30 – 4:10 p.m.	40	Pros and Cons of Multi-Targeted Therapeutics	*Moderator:* Edward Cha, MD, PhD – *Genentech* *Panelists:* Raphael Clynes, MD, PhD – *Xencor, Inc.* David S. Hong, MD – *The University of Texas MD Anderson Cancer Center* Jeffrey S. Miller, MD – *University of Minnesota* Israel Lowy, MD, PhD – *Regeneron Pharmaceuticals* Marcela V. Maus, MD, PhD – *Massachusetts General Hospital*

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Session 2: Novel Platforms and Innovation				
Application 1	4:10-4:20 p.m.	10	Contextual reprogramming of T cells for multi-targeted therapeutics: checkpoint blockade, immune resilience, and stemness to overcome immune resistance and reduce toxicity, all in one cell product	Francesco M. Marincola, MD – *Refuge Biotechnologies*
Application 2	4:20-4:30 p.m.	10	The first personalized adoptive cellular therapy trial using defined multiple targets (ACTolog IMA101-101)	Steffen Walter, PhD – *Immatics US*
Application 3	4:30-4:40 p.m.	10	A novel fully synthetic dual targeted Nectin-4/4-1BB Bicycle® peptide induces tumor localized 4-1BB agonism	Nicholas Keen, PhD – *Bicycle Therapeutics*
Application 4	4:40-4:50 p.m.	10	Combining CD27 costimulation and PD-1 blockade into a bispecific antibody improves T cell activation and anti-tumor activity over combination of individual antibodies	Tibor Keler, PhD – *Celldex Therapeutics, Inc.*
Application 5	4:50-5:00 p.m.	10	Development of novel multi-specific compounds for cancer immunotherapy using the DARPin® technology platform	Victor Levitsky, MD, PhD – *Molecular Partners AG*
Application 6	5:00-5:10 p.m.	10	The uniqueness and persistence of clonal profiles associated with response in study C-144-01 following treatment with lifileucel (LN-144) supports using a polyclonal product to treat solid tumors	Viktoria Gontcharova, PhD – *Iovance Biotherapeutics*

Session 3: Clinical Applications of Multi-Targeted Therapeutic Platforms				
Faculty	5:25-5:45 p.m.	20	Clinical Trial Designs	R. Angelo De Claro, MD – *Food and Drug Administration*
Panel Discussion	5:45 – 6:25 p.m.	40	Compare and Contrast with Cellular Therapies Panel Discussion	*Moderator:* Leena Gandhi, MD, PhD – *Eli Lilly* R. Angelo De Claro, MD – *Food and Drug Administration* Viktoria Gontcharova, PhD – *Iovance Biotherapeutics* Victor Levitsky, MD, PhD – *Molecular Partners AG* Nicholas Keen, PhD – *Bicycle Therapeutics* Tibor Keler, PhD – *Celldex Therapeutics, Inc.*

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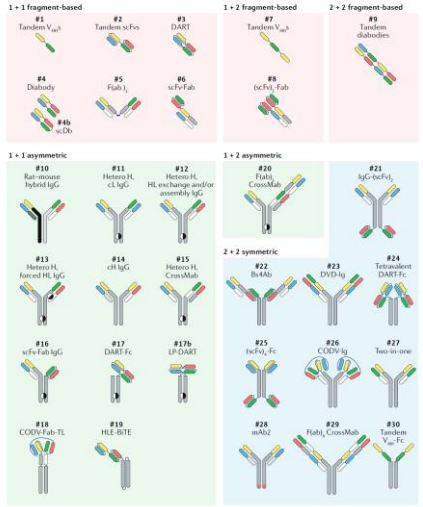
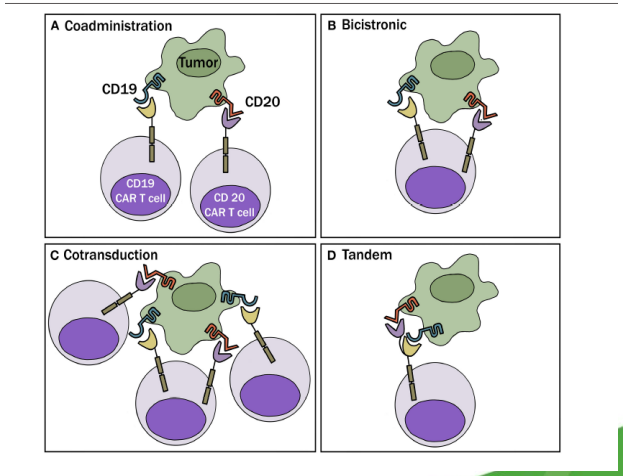
Definition: what do we mean for multi-targeted therapeutic?

- A single therapeutic engaging multiple targets/specificities (spatially, temporally):
  - Examples:

Polispecific monoclonal antibodies



Multi-targeted CAR-T cells



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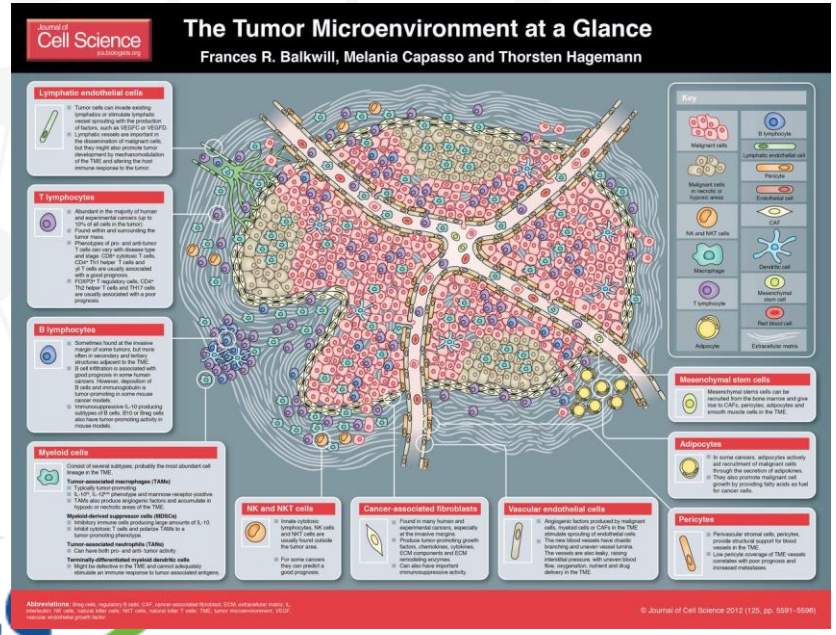
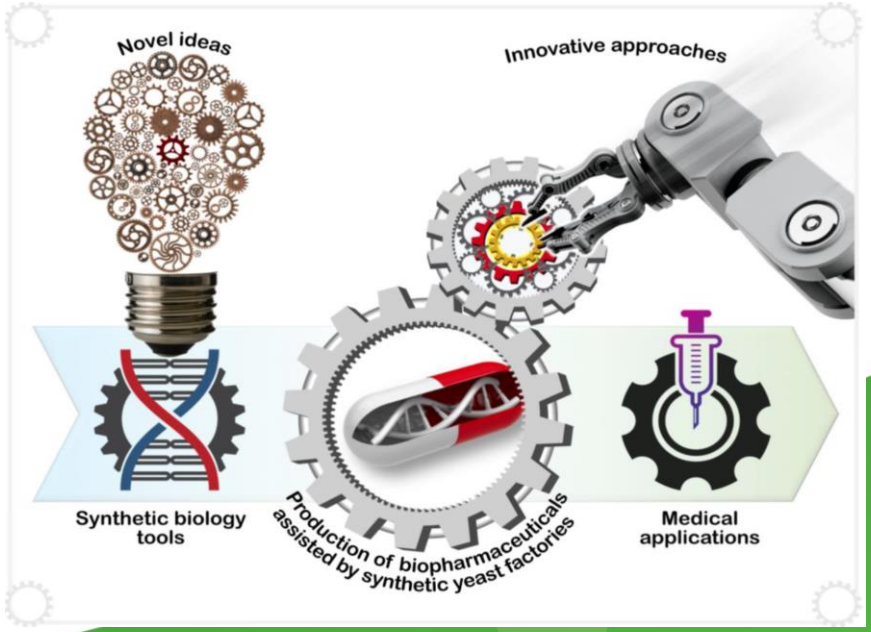
Why the “surge” in Multi-targeted therapeutics in IO?

Growing understanding of cancer immune-response and *its multi-facet nature*



Availability of “synthetic biology” tools for protein and cells engineering



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Multi-targeted therapeutics: *when the whole is great than the sum of the parts*

- Despite the great variety of multi-targeted therapeutics it is useful to classify them from a mechanistic perspective

  - *Combinatorial design*: the poli-specific therapeutic is intended as an alternate to the mixture of two mono-specific therapeutics (e.g. anti-PD-1/LAG3)

  - *Obligate design*: the physical linkage of the binding domains create *a new functionality (spatial or temporal)* which cannot be accomplish by a mixture of the two mono-specific therapeutics

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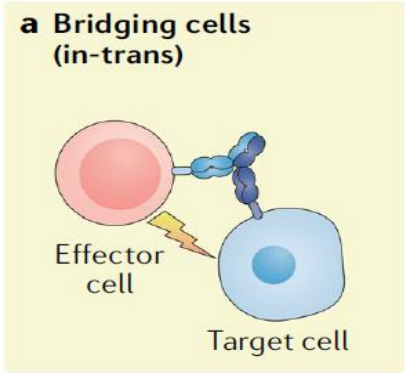
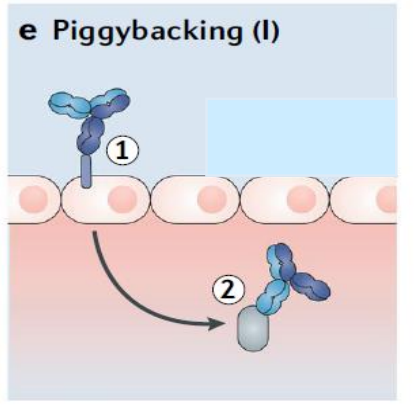
Examples of obligate mechanisms of action of bispecific Abs

- T-cell redirection (BiTEs):
  - 56 compounds in active clinical trials and 1 marketed
- Beyond T cells:
  - NK cells (2 CD16 x TAA in Phase II)- BiKEs and TRiKEs

- Cytokine-Antibody fusion proteins;
  - Exploiting antibodies for cytokine delivery (sequential binding)





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