

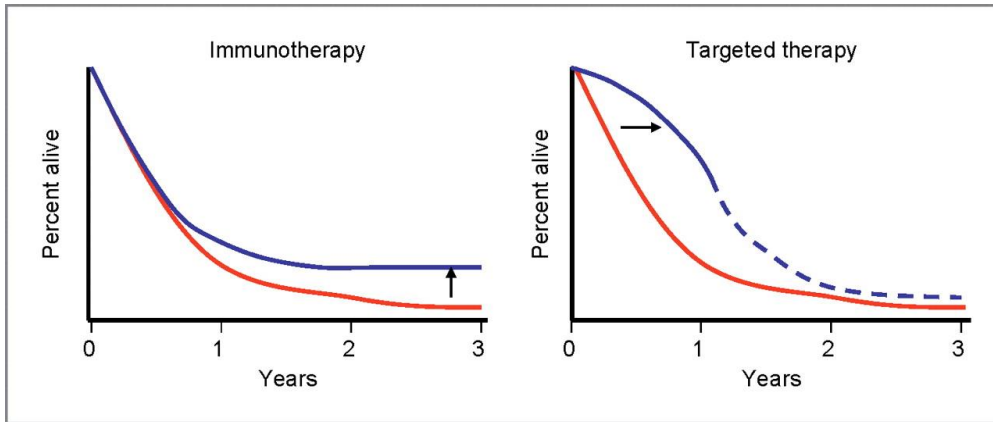
Challenges, Insights, and Future Directions for Experimental Models in Cancer Immunotherapy

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Outline:

- ▶ Introduction to cancer Immunotherapy
- ▶ Mouse models for cancer Immunotherapy
- ▶ Managing outsourced vendors effectively

Different Therapeutic Approaches, Different Benefit Measures

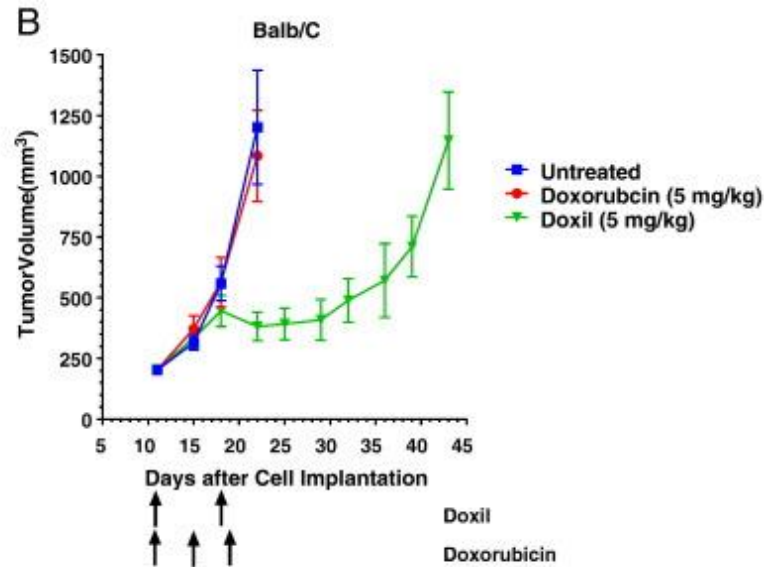
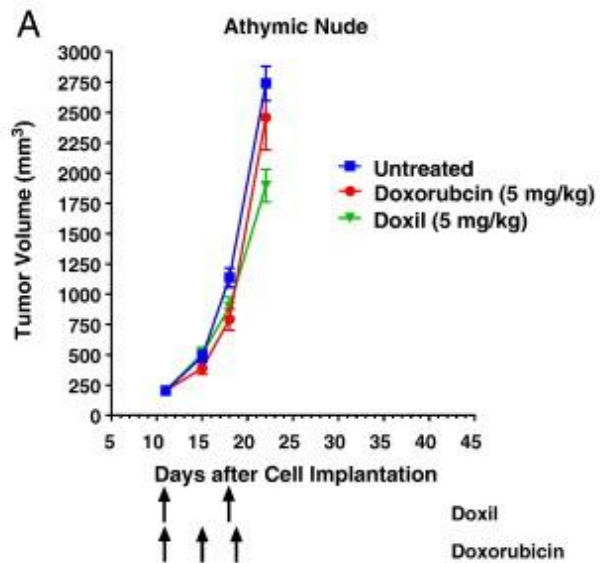


Antoni Ribas et al. Clin Cancer Res 2012;18:336-341

► Immunotherapy strategies have the notorious ability to induce a low percentage but highly durable tumor responses, resulting in a plateau in the tail of the survival curve.

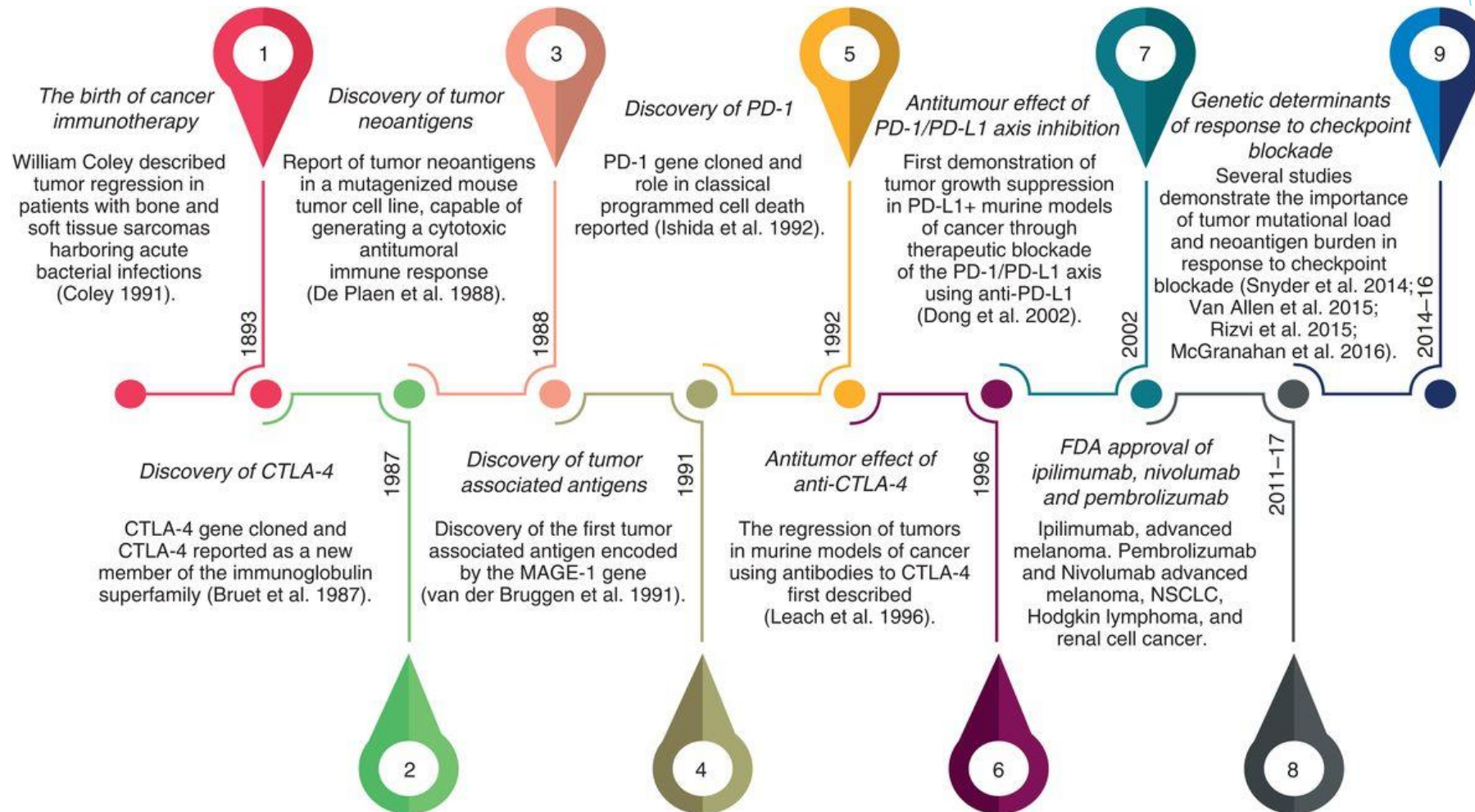
► Targeted therapy blocking driver oncogenes in cancer induces rapid tumor responses, but most are not durable, resulting in an early improvement in the survival curve but unclear beneficial effects on the tail of the curve.

Immune system can improve chemotherapeutics, in some cases



Doxil was active when CT26 tumors were grown in immunocompetent mice but not immunocompromised mice, demonstrating that Doxil activity is increased in the presence of a functional immune system

Key Milestones in Cancer Immunotherapy



The Founding Principals of the Immunotherapy of Cancer

1

The demonstration of immuno-surveillance using immune - deficient mouse models

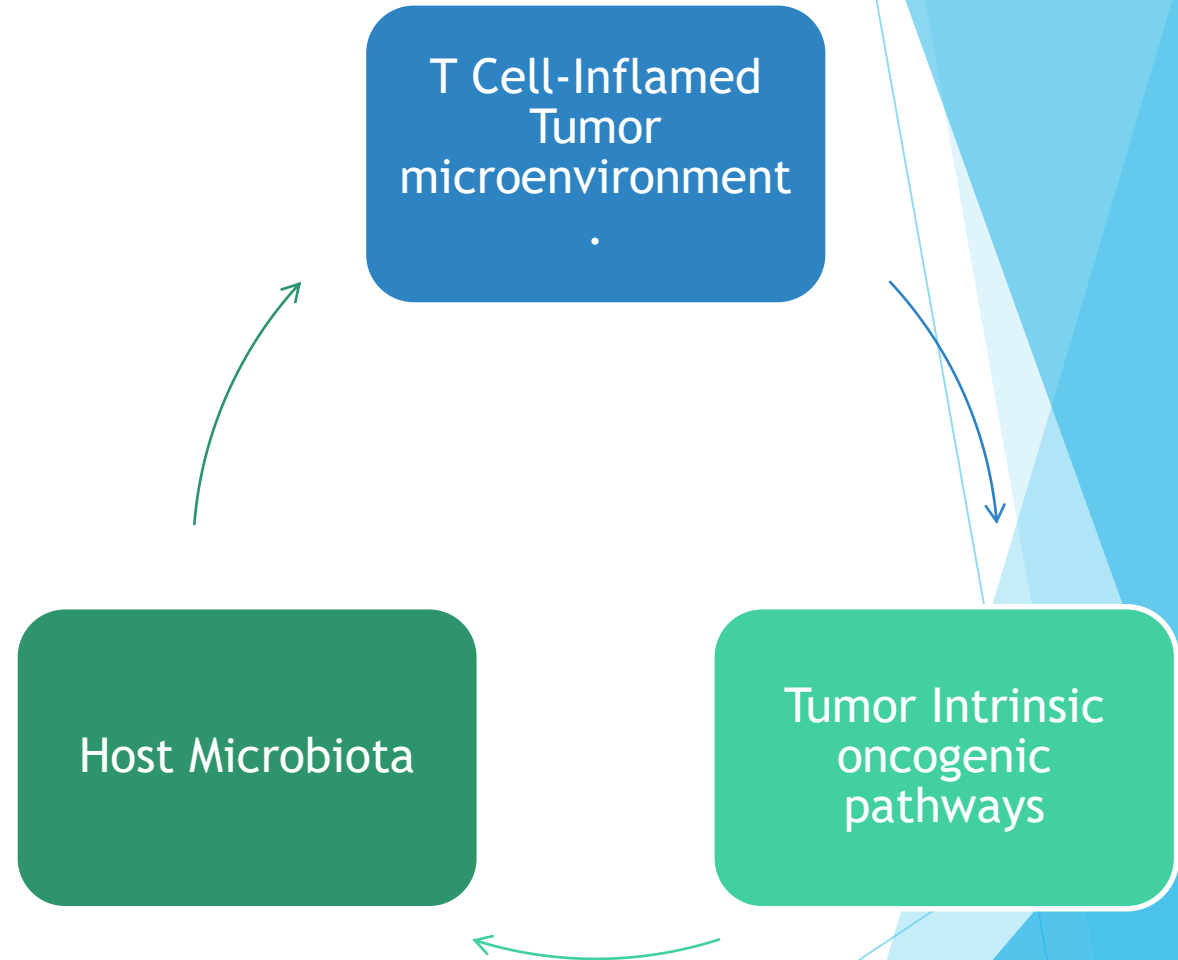
2

The demonstration of the major importance of pre-existing immunity and natural intratumoural T cells in humans

3

The unleashing of pre-existing immunity via inhibition of checkpoint receptors on T cells in human cells

Factors Controlling Antitumor Immunity and Efficacy of Cancer Immunotherapy



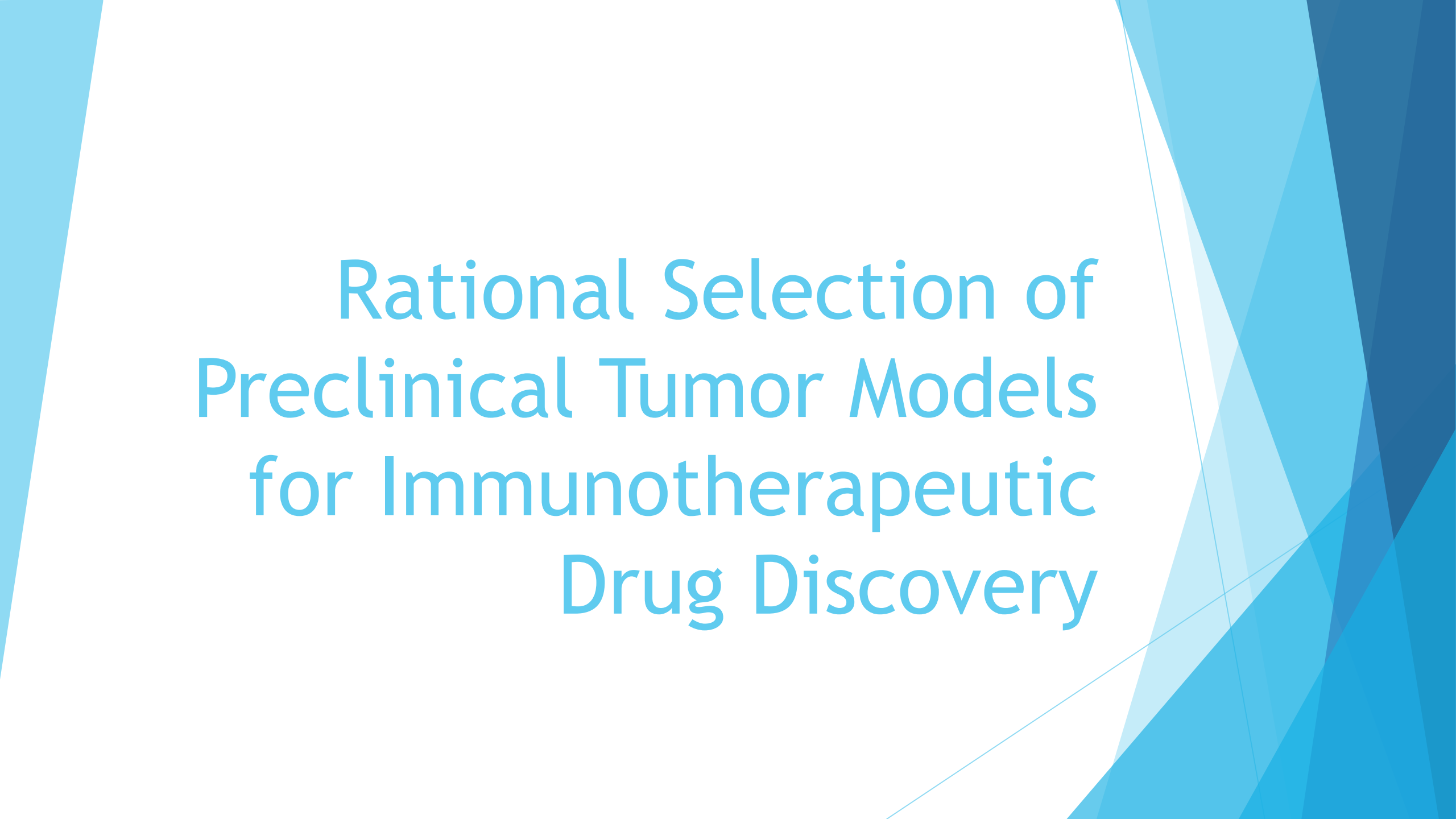
ImmunoOncology Discovery Platforms

2D and 3D
(Organoids) *in vitro* functional
assays

Syngeneic *in vivo*
tumor models

Humanized
mouse models
(PDX)

Crisper/Cas9
genome editing
in vitro and *in vivo*

The background features abstract, overlapping geometric shapes in various shades of blue, ranging from light sky blue to deep navy blue. The shapes are primarily triangles and polygons, creating a dynamic, layered effect. The text is centered in the white space between these shapes.

Rational Selection of Preclinical Tumor Models for Immunotherapeutic Drug Discovery

Summary of Syngeneic Models

Advantages

Reproducible and rapid growth

Easily manipulated

No host breeding requirement

Disadvantages

Lack of native tumor microenvironment

Variability of phenotype depending on the site of engraftment

Relatively few transplantable cell lines

Lack of heterogeneity

Relatively few cell lines and host strains

Managing Outsourced

- ▶ Vendors Effectively

Internal Vs. External Sources

INTERNAL

Attention should be given to the critical activities and the activities that the company has distinctive expertise at.

OUTSOURCING

Vendors should be contacted based on their distinct and comparative skills, greater work scale, cost and project timeline

When should the technical assessment be performed?

- ▶ Prior to using a CRO for the first time
- ▶ If using a CRO again after a period of not using the CRO
- ▶ On an annual basis (depending on how often the lab is used)

Confidential Agreement

- ▶ Prepare a **Confidential Disclosure Agreement (CDA)** template
- ▶ Two way (mutual) is the easiest
- ▶ Have your legal department review and sign



Routine Study Monitoring



Directed Investigation



Communication and Risk Assessment

Communication and Coordination



Risk Management



Outsourcing Overload

