Workshop Imunoterapia

Ana Ramos Coelho, Ph.D.

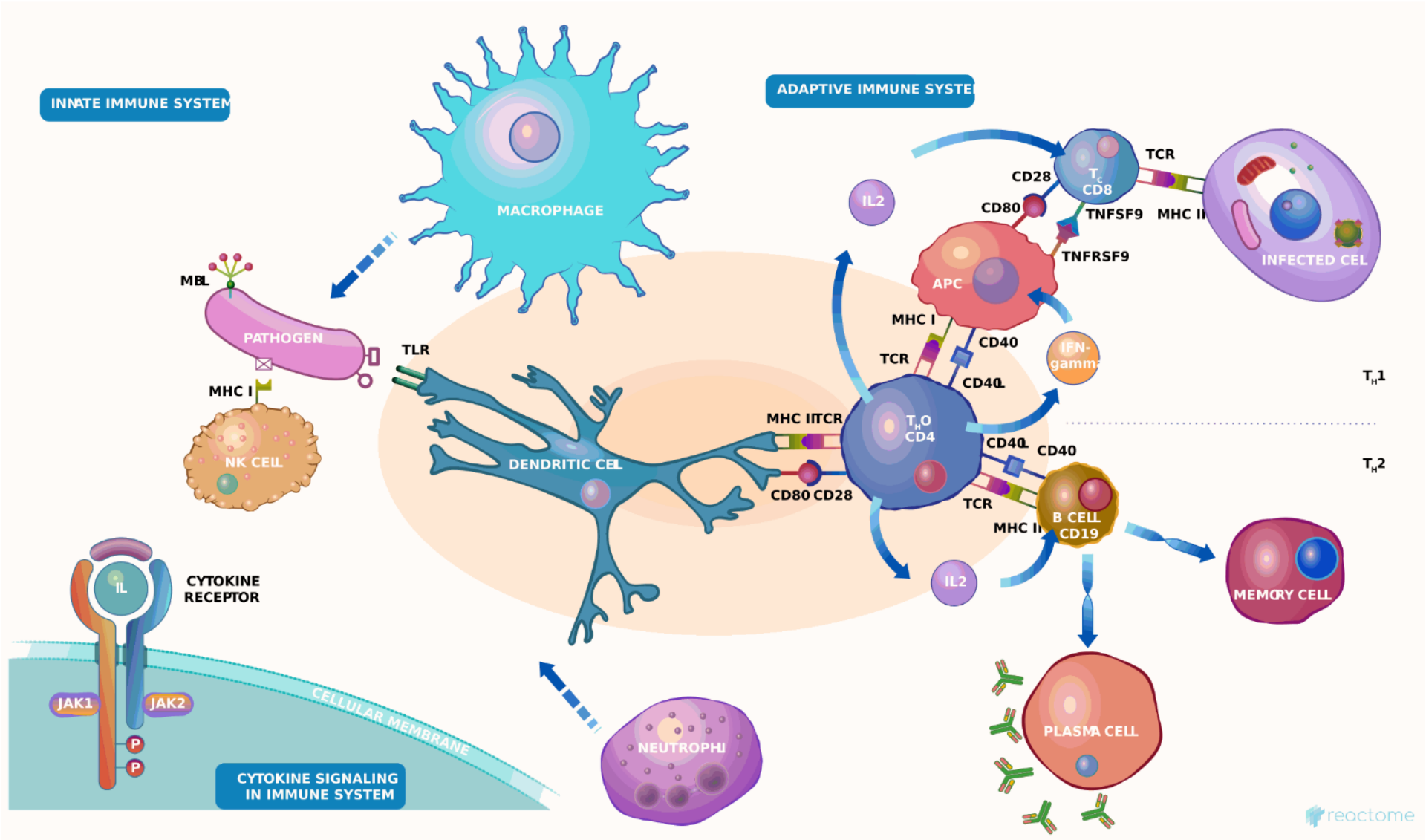
[1] Escola Superior de Tecnologia da Saúde de Lisboa, ESTeSL, Instituto Politécnico de Lisboa, Av. D. João II, Lote 4.69.01, 1990-096 Lisboa, Portugal, ana.ramos@estesl.ipl.pt

[2] H&TRC - Centro de Investigação em Saúde e Tecnologia

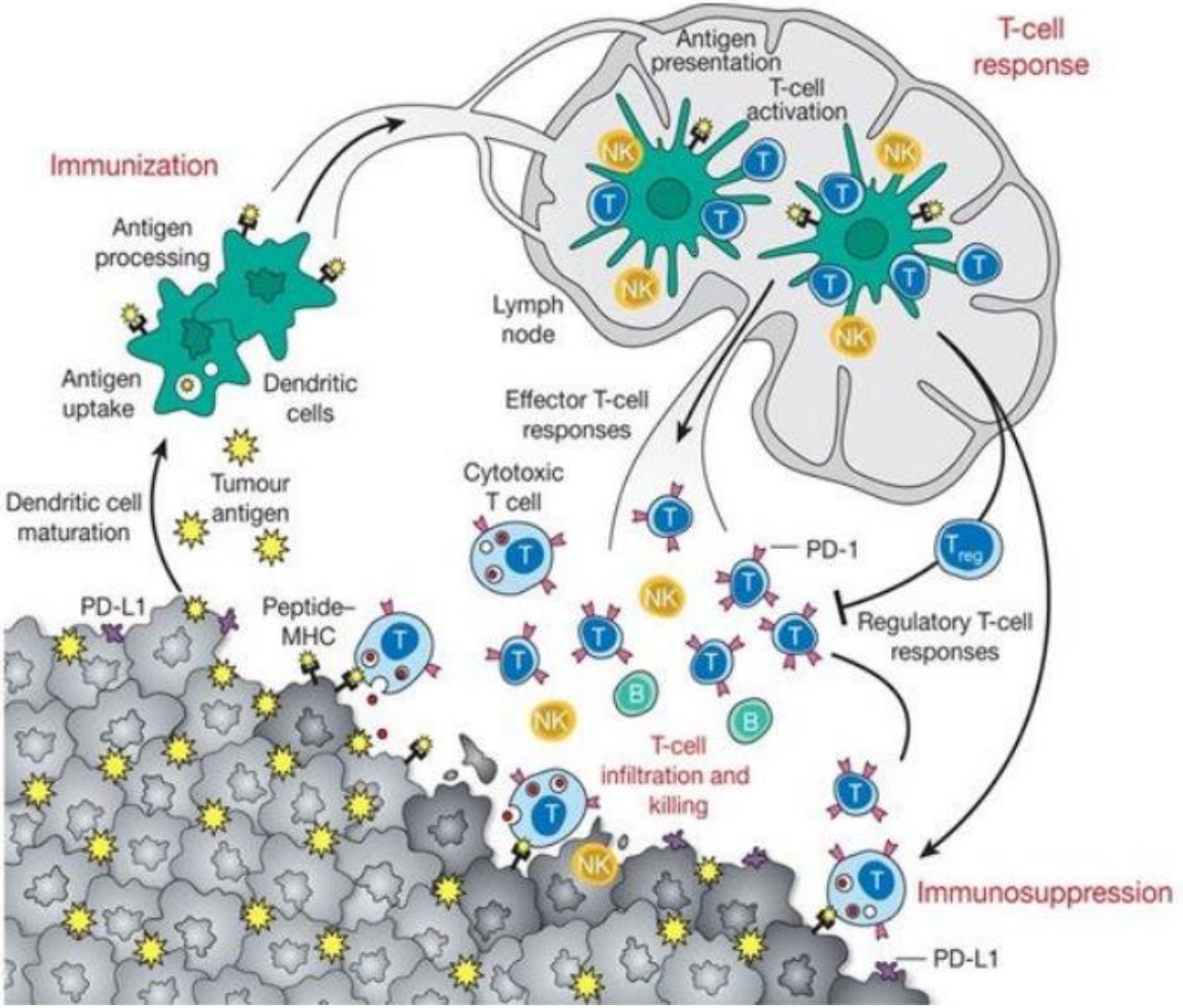
III Congresso Nacional em Ciências Biomédicas Laboratoriais

25 outubro de 2019

Sistema Imunitário

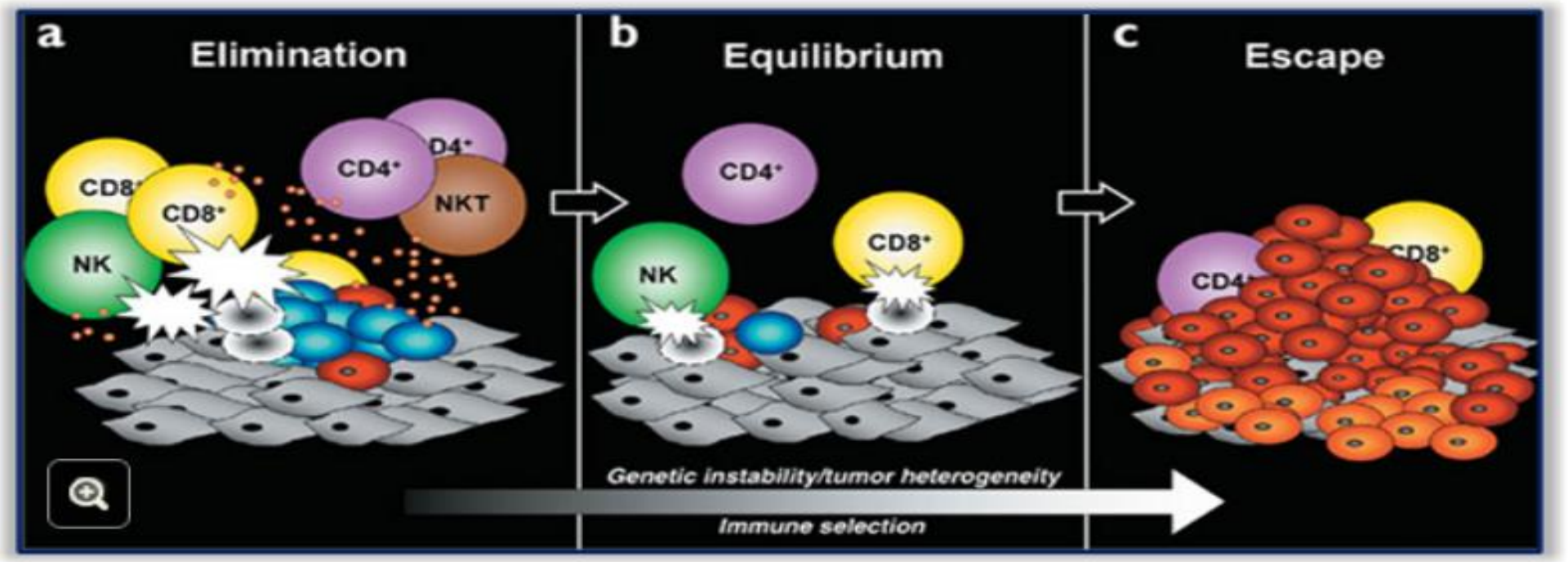


Reconhecimento tumoral



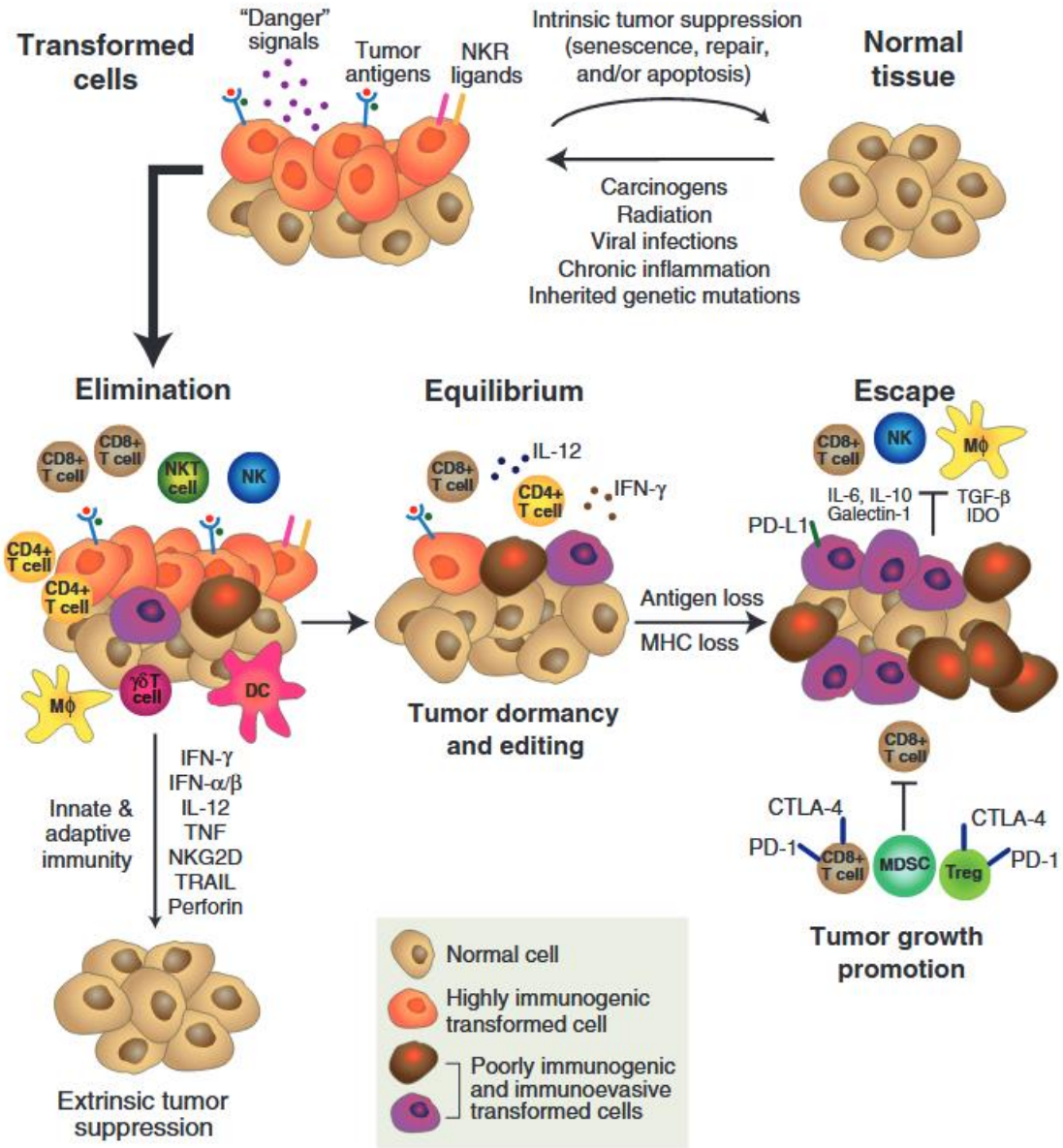
Mellman I et al. Nature 2011

Cancer Imunoediting



Dunn GP et al. Nat Immunol. 2002

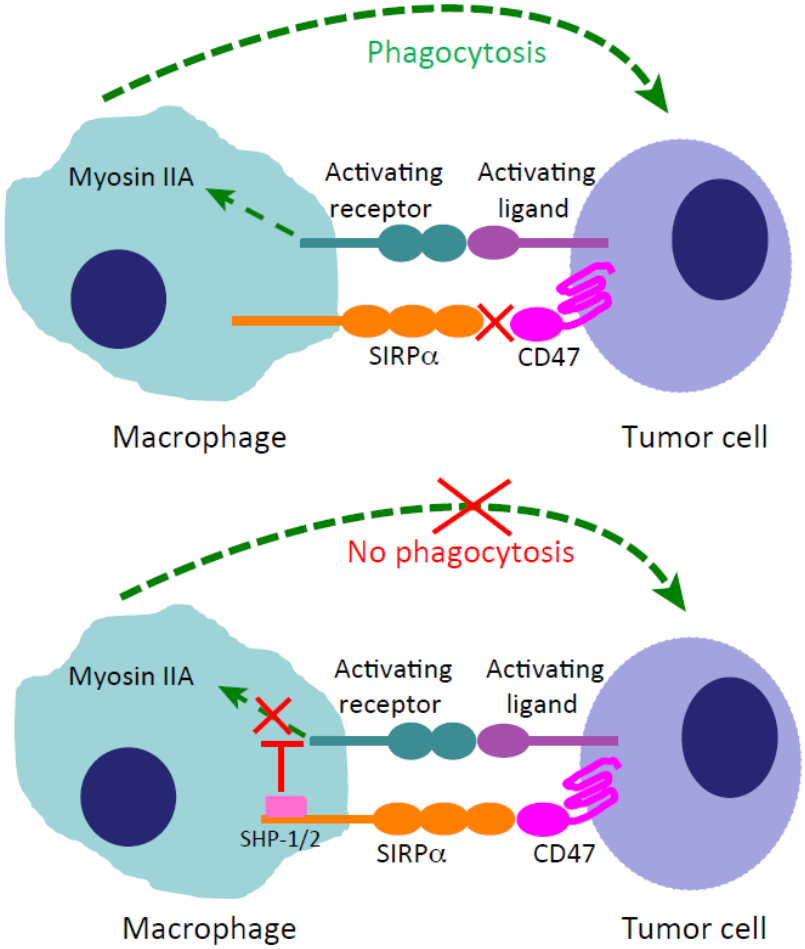
Cancer Imunoediting



Schreiber R et al. Science 2011

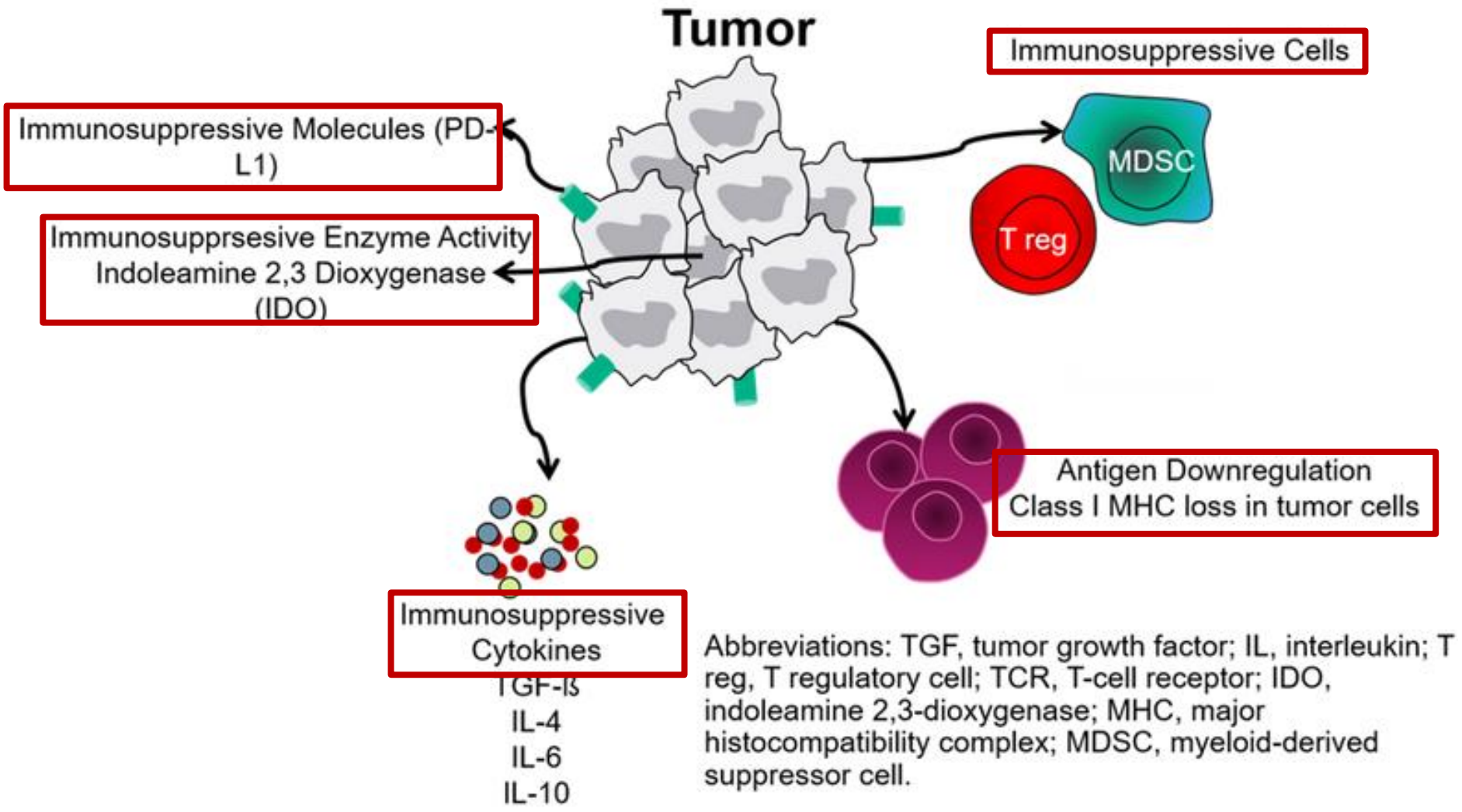
Evasão à imunidade inata

- SIRPα – macrófagos, células dendríticas e neutrófilos



Veillette and Chen Trends in Immunology 2018

Evasão à imunidade adaptativa



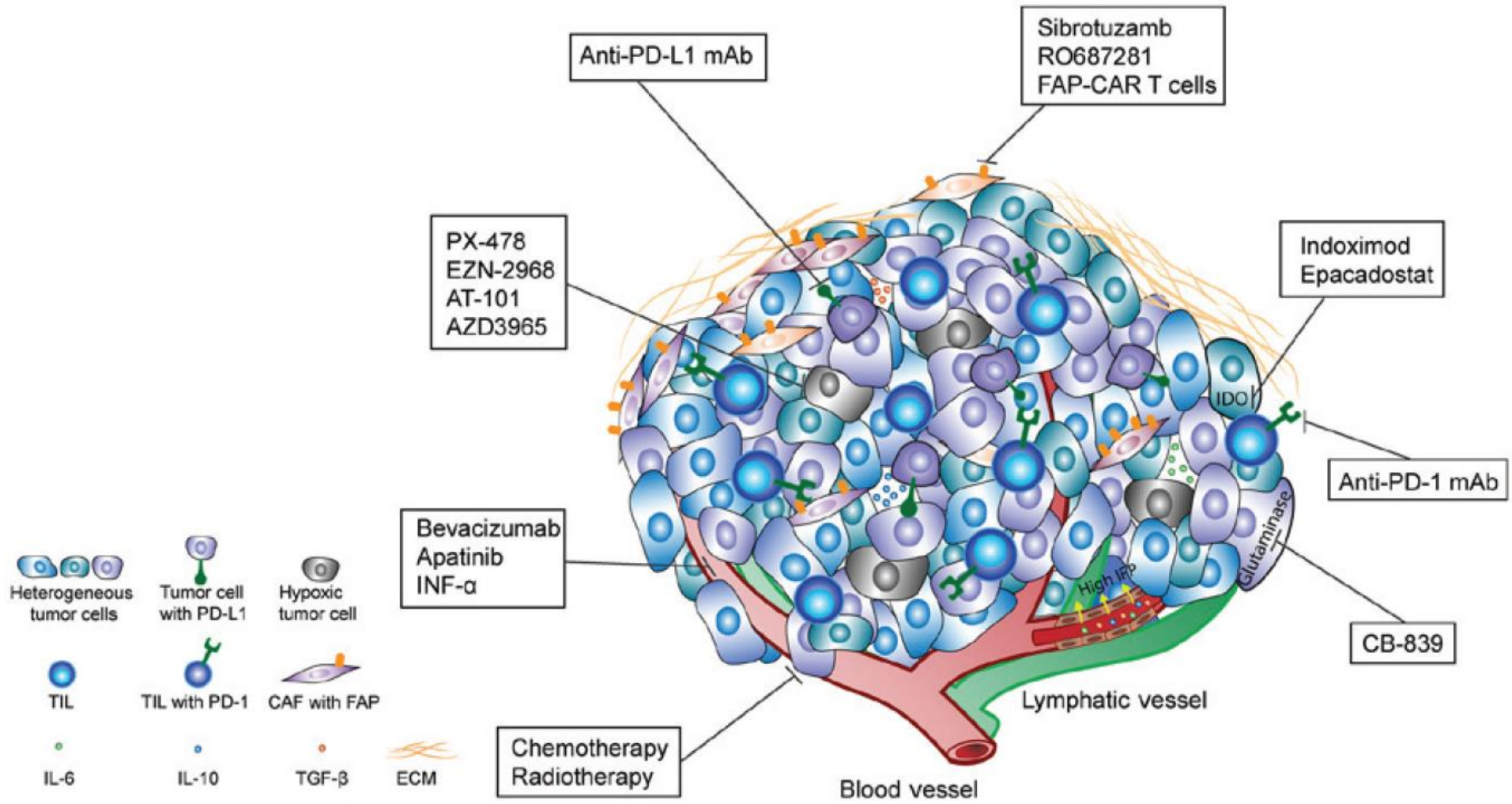
Abbreviations: TGF, tumor growth factor; IL, interleukin; T reg, T regulatory cell; TCR, T-cell receptor; IDO, indoleamine 2,3-dioxygenase; MHC, major histocompatibility complex; MDSC, myeloid-derived suppressor cell.

Weiner N Engl J Med. 2008

Estratégias Imunoterapia em Cancro

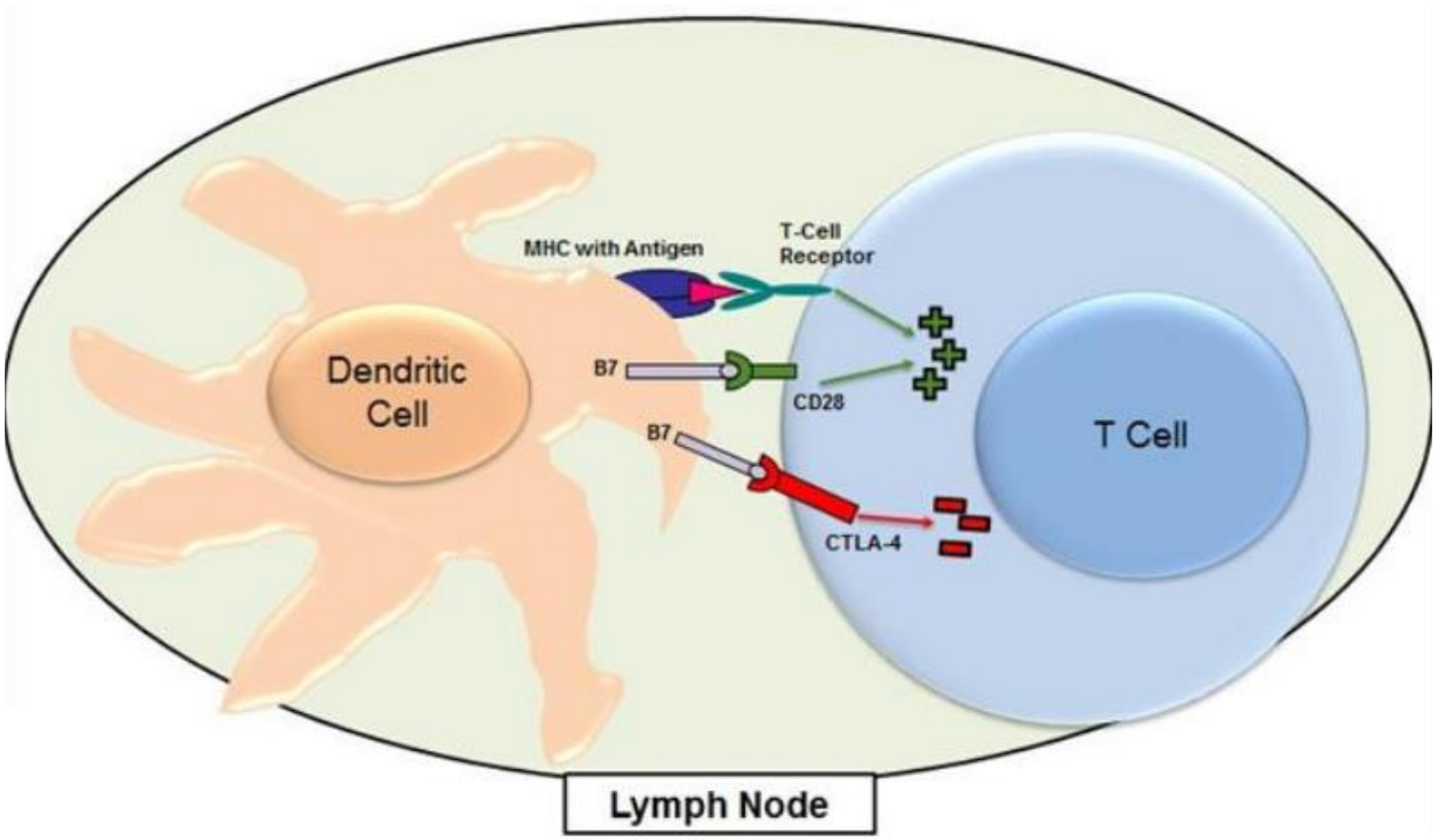
- Anticorpos imunoreguladores: bloqueio de inibidores sistema imunitário
- Adoptive Cell Therapy
- Citoquinas
- Vacinas

Estratégias Imunoterapia em Cancro



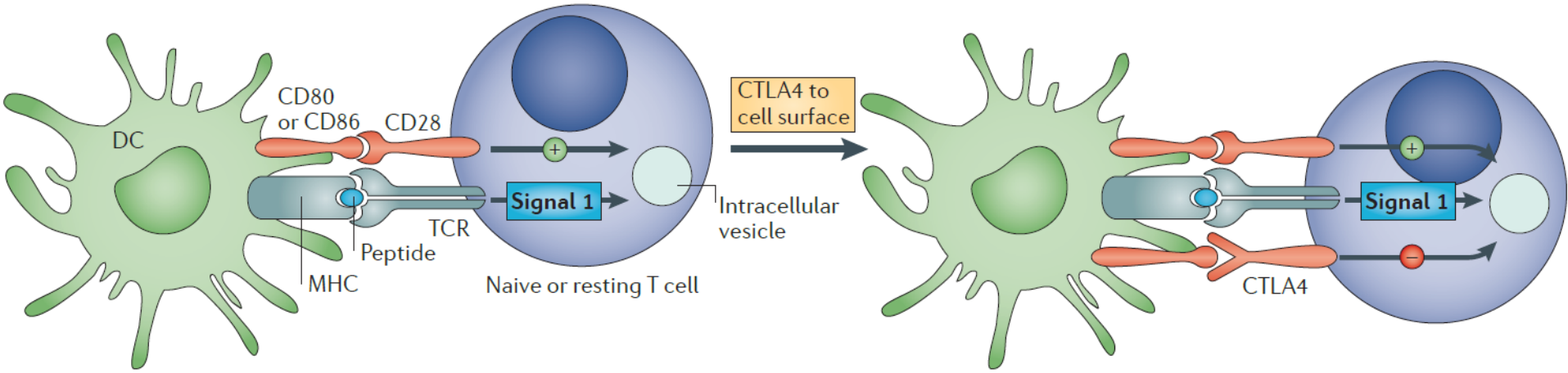
Yu Y and Cui J Oncol Lett. 2018

CTLA-4



Postow MA, et al. J Clin Oncol. 2015

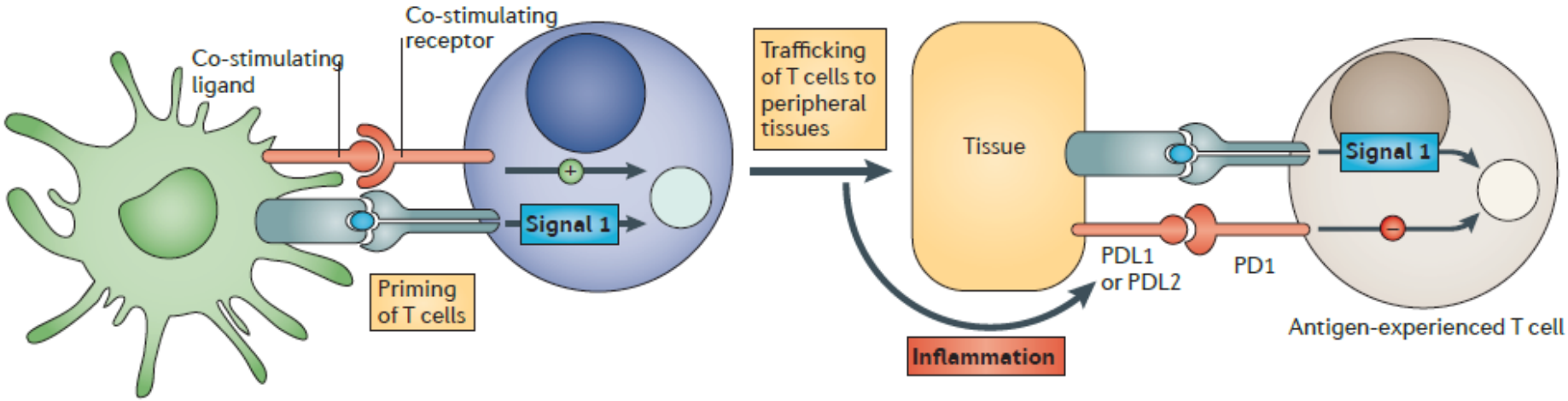
CTLA-4



Pardol DM. Nat Rev Canc 2012

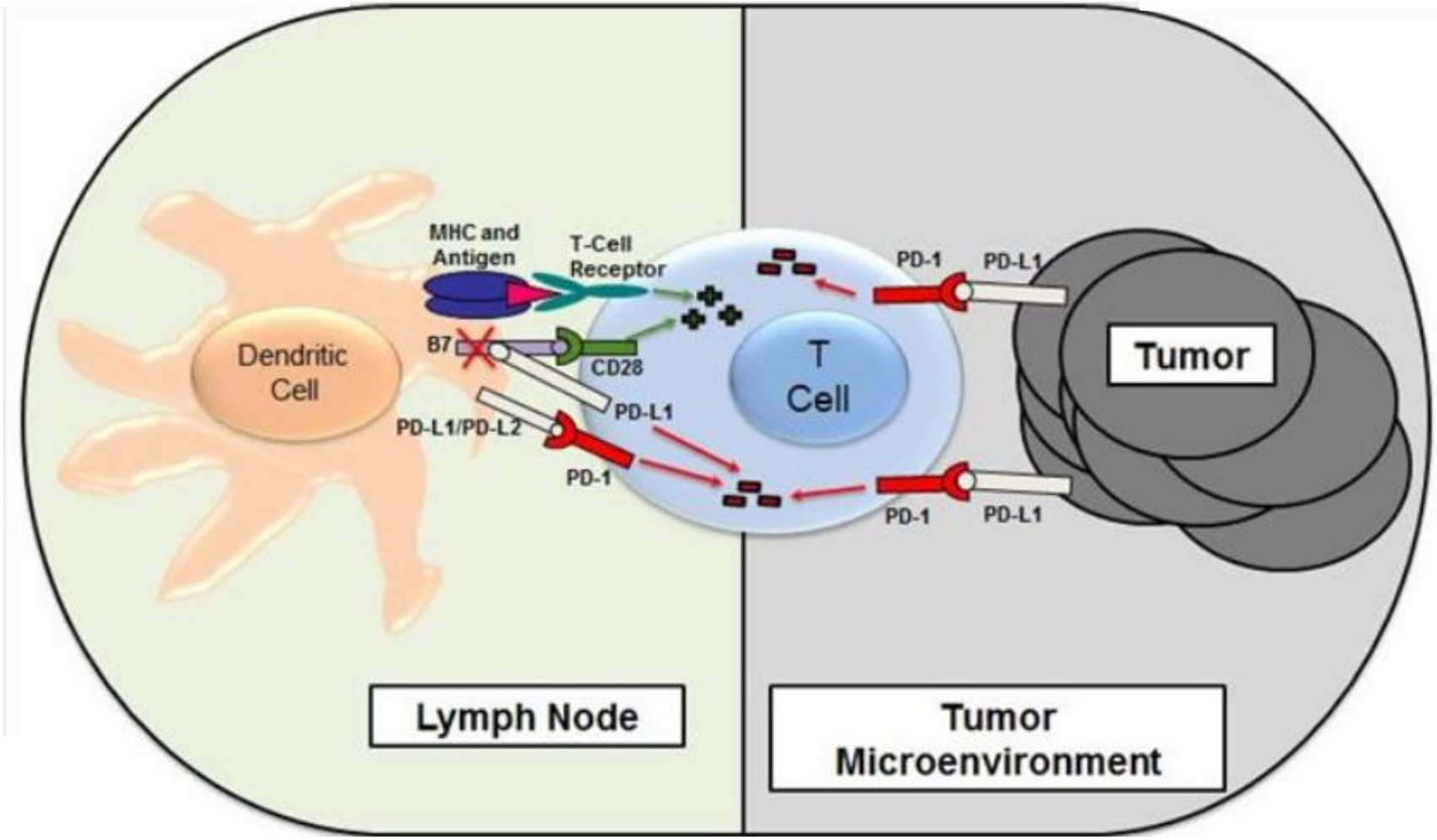
- CTLA-4 sequestrado em vesículas intracelulares é transportado para a superfície.

PD-1

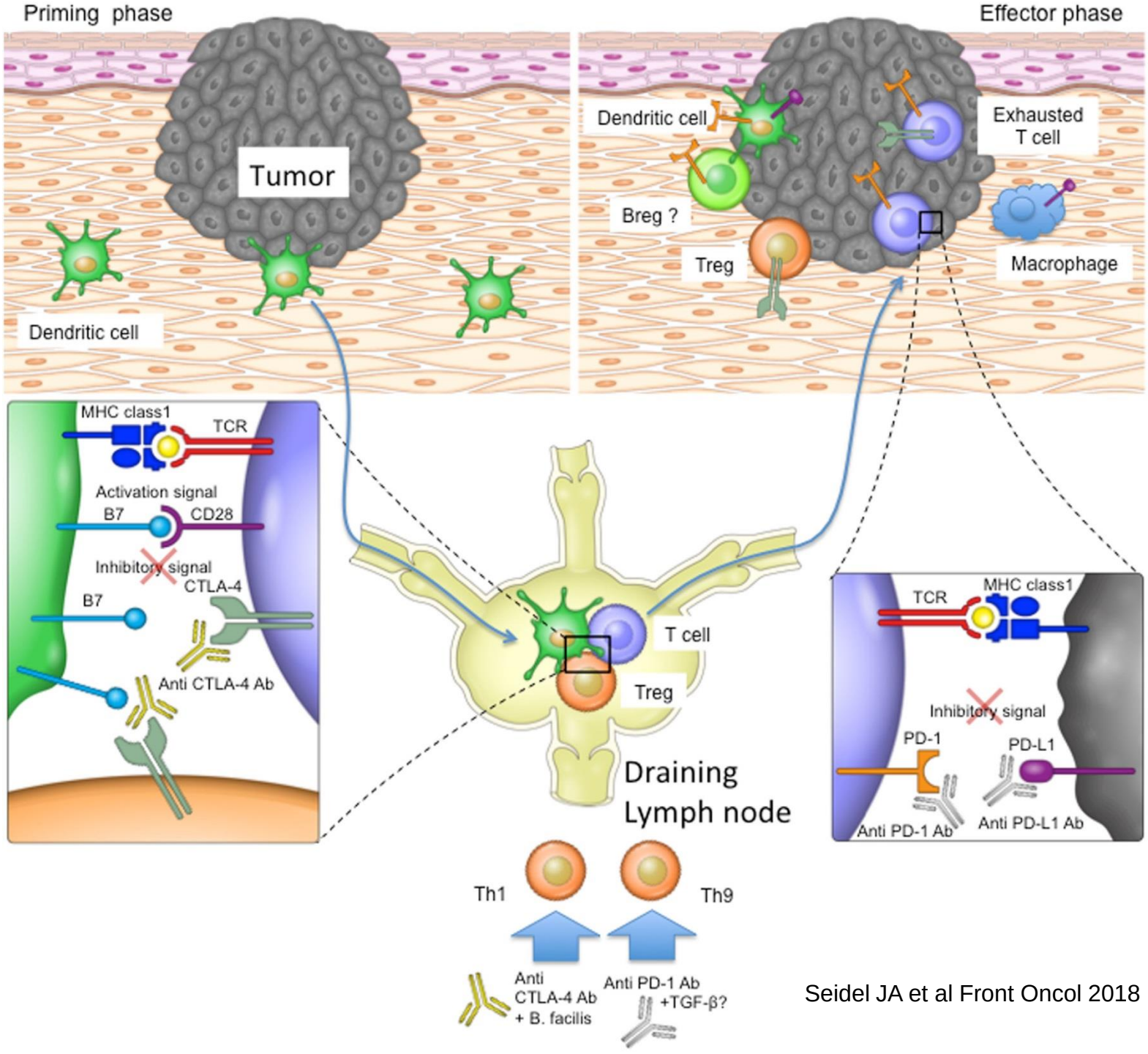


Pardol DM. Nat Rev Canc 2012

PD-1



Postow MA, et al. J Clin Oncol. 2015



Seidel JA et al Front Oncol 2018

Bloqueio dos checkpoints imunes

Target	Biological function	Antibody or Ig fusion protein
CTLA4	Inhibitory receptor	Ipilimumab
		Tremelimumab
PD1	Inhibitory receptor	MDX-1106 (also known as BMS-936558)
		MK3475
		CT-011‡
		AMP-224§
PDL1	Ligand for PD1	MDX-1105
		Multiple mAbs
LAG3	Inhibitory receptor	IMP321‖
		Multiple mAbs
B7-H3	Inhibitory ligand	MGA271
B7-H4	Inhibitory ligand	
TIM3	Inhibitory receptor	

Pardol DM. Nat Rev Canc 2012

Bloqueio dos checkpoints imunes

- **CTLA-4:** Melanoma, carcinoma pulmão não-pequenas células
- **PD-1:** Melanoma, carcinoma renal metastático, linfoma de Hodgkin, cancro pulmão não-pequenas células, cancro ovário, cancro da bexiga, CRC metastático, linfoma células B
- **CTLA-4 + PD-1:** Melanoma V600 WT
- **PD-1 + Tim-3**
- **PD-1 + LAG-3**

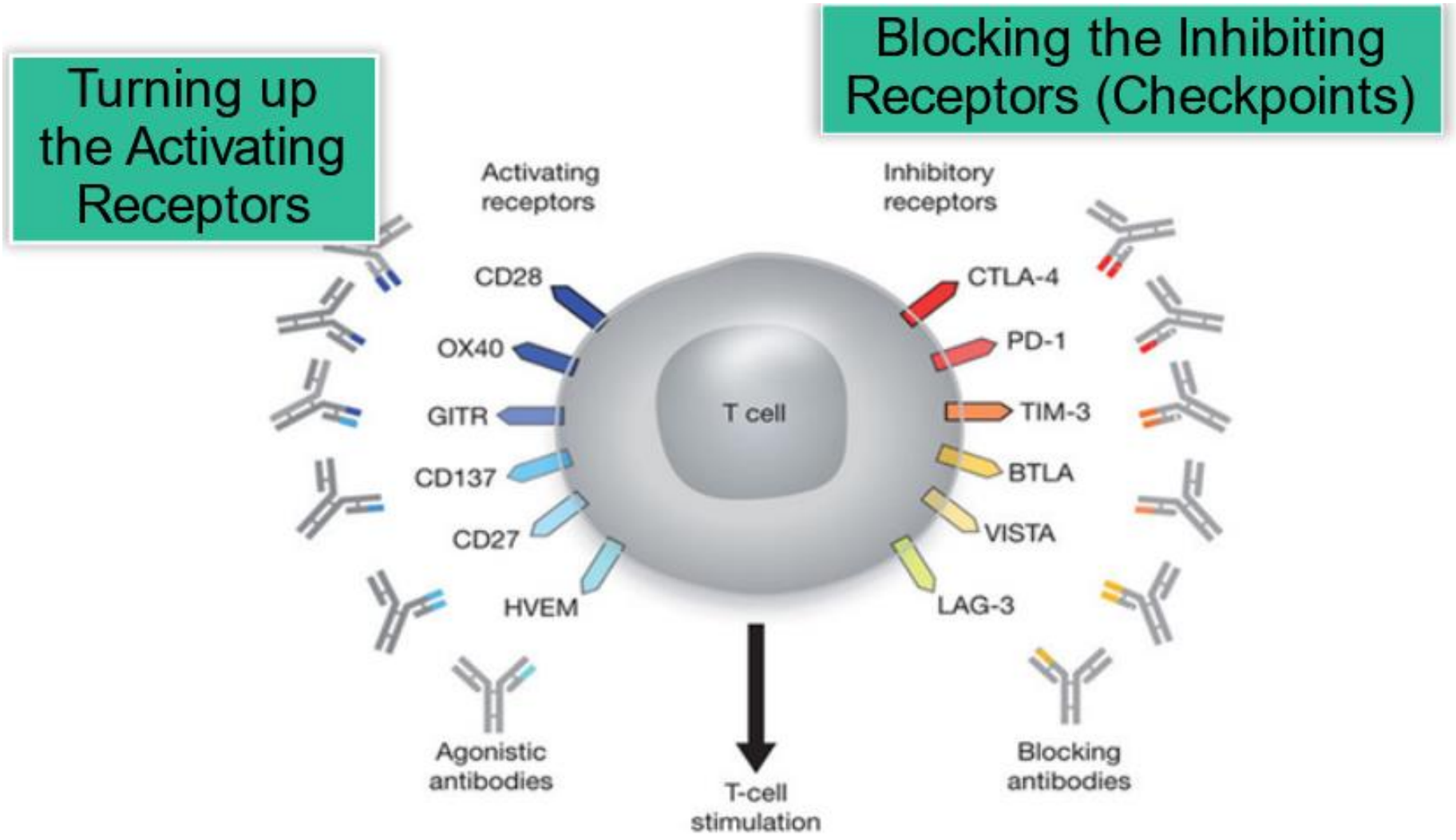
Bloqueio dos checkpoints imunes

TABLE 3 | Biomarkers associated with favorable responses to immune checkpoint inhibitors.

	Pre-treatment	**Post-treatment**
Tumor	Tumor size and distribution (66) High mutation burden but no innate anti-PD-1 resistance (IPRES) gene signature (78, 86, 87, 96) PD-L1 expression on tumor cells (only confirmed by some but not all studies) (67, 108)	Reduction in tumor size
Tumor-infiltrating immune cells	Presence of CD8 + T cells inside the tumor or at the tumor margin (88) PD-L1 expression by infiltrating cells (77) Increased Th1- and CTLA-4-associated gene expression (77).	Proliferation of intratumoral CD8 + T cells (88)
Circulation	High relative lymphocyte counts (109) High relative eosinophil counts (109) High serum TGF-β levels (91, 92) Low serum LDH levels (66, 109) Low levels of ctDNA (107)	Increased levels of ICOS + T cells (110) Low neutrophil-to-lymphocyte ratio (110) High levels of Th9 cells A reduction in serum LDH levels (104) A reduction in ctDNA (107)
Host genome	Presence of HLA-A*26 allele (111)	

Seidel JA et al Front Oncol 2018

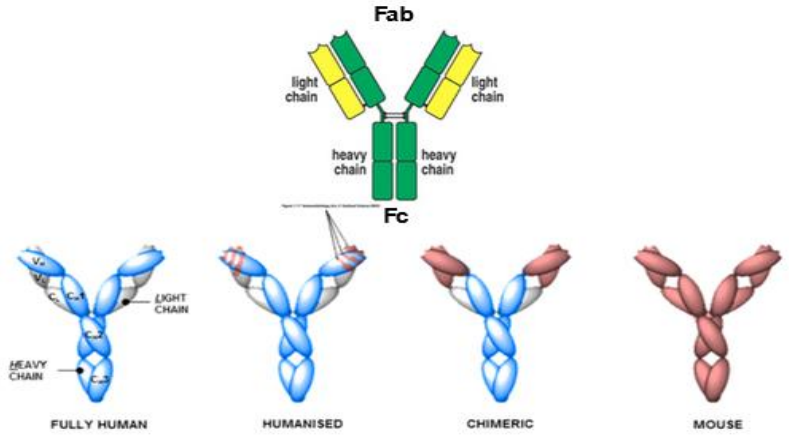
Regulação das células T



Mellman I et al. Nature 2011

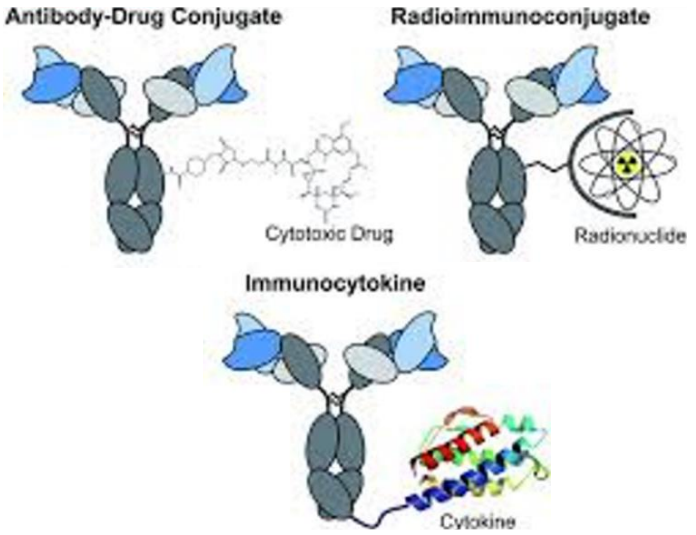
Anticorpos

- Humanizados



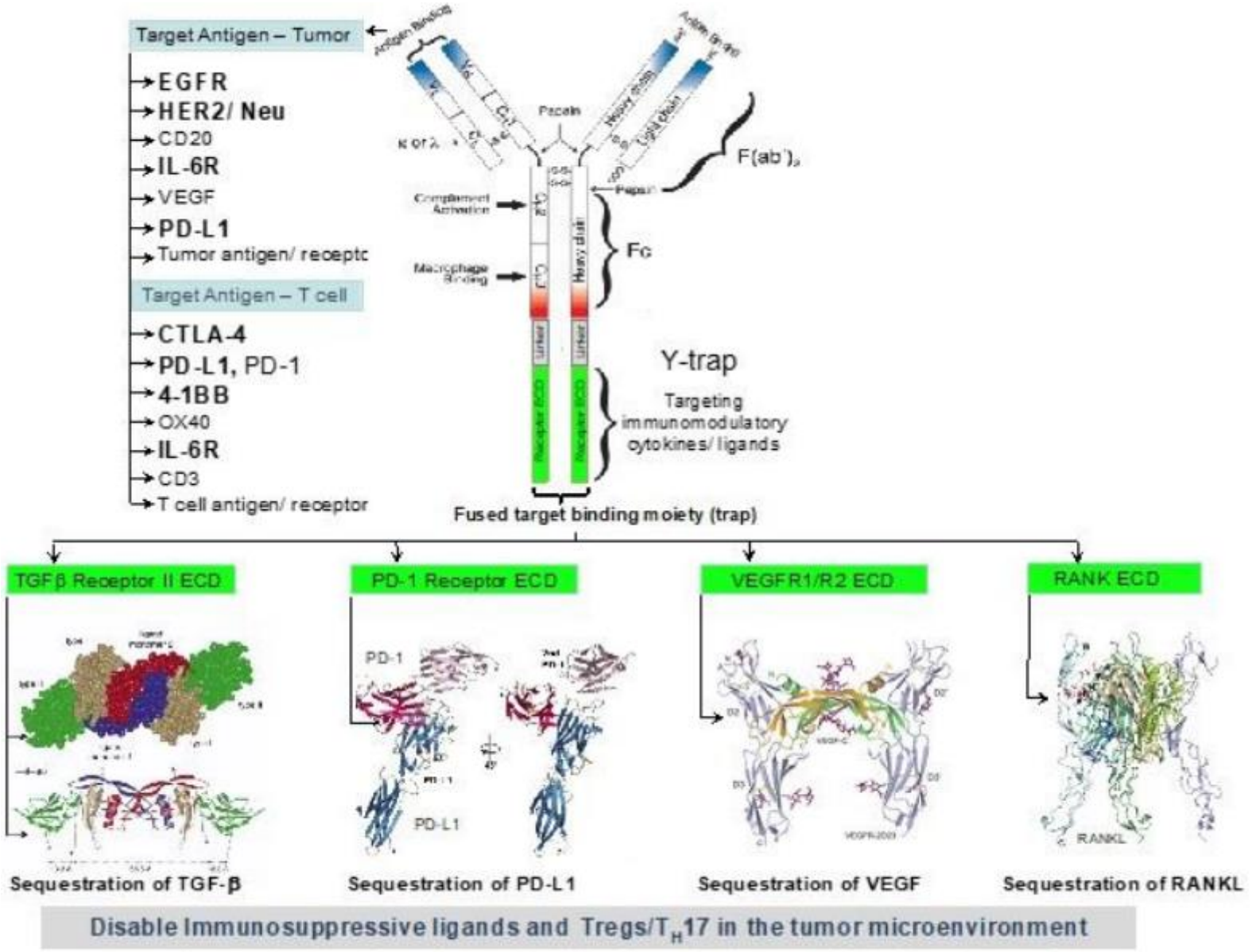
Hess C, et al. Med Chem Commun. 2014

- Ligados a outros agentes



Hess C, et al. Med Chem Commun. 2014

Anticorpos


Target Antigen – Tumor
EGFR
HER2/ Neu
CD20
IL-6R
VEGF
PD-L1
Tumor antigen/ receptc
Target Antigen – T cell
CTLA-4
PD-L1, PD-1
4-1BB
OX40
IL-6R
CD3
T cell antigen/ receptor
Papain
F(ab')2
Fc
Y-trap
Targeting
immunomodulatory
cytokines/ ligands
Fused target binding moiety (trap)
TGFβ Receptor II ECD
PD-1 Receptor ECD
VEGFR1/R2 ECD
RANK ECD
PD-1
PD-L1
RANKL
Sequestration of TGF-β
Sequestration of PD-L1
Sequestration of VEGF
Sequestration of RANKL
Disable Immunosuppressive ligands and Tregs/T$_H$17 in the tumor microenvironment

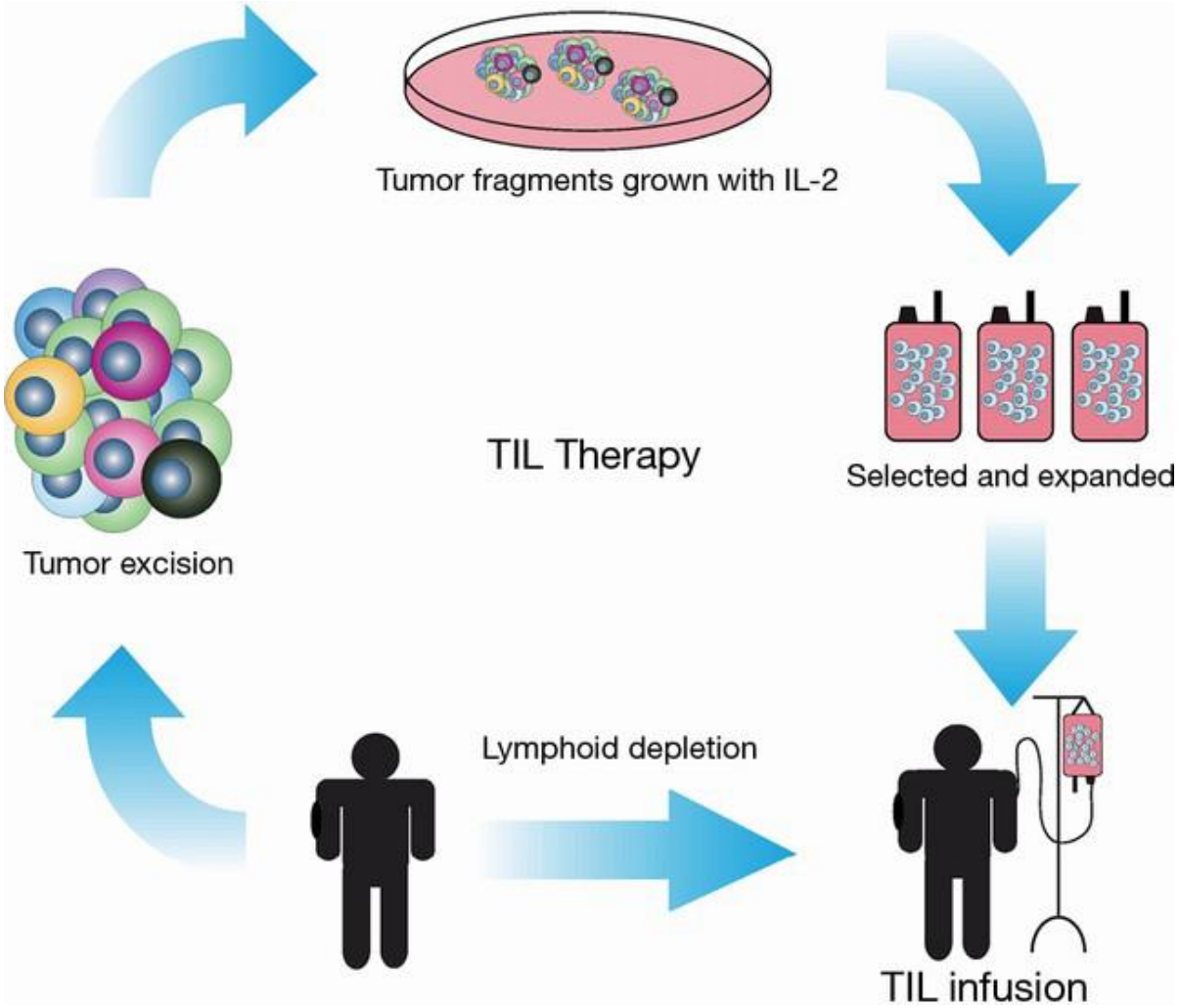
Adoptive Cell Therapy

1. Tumor-infiltrating lymphocytes (TIL)

2. T cells expressing novel TCRs

3. T cells expression chimeric antigen receptors (CAR)

TIL



- Expansão ex vivo de TILs do MAT e transferência

TIL

Published in final edited form as:
Clin Cancer Res. 2011 July 1; 17(13): 4550–4557. doi:10.1158/1078-0432.CCR-11-0116.

Durable Complete Responses in Heavily Pretreated Patients with Metastatic Melanoma Using T Cell Transfer Immunotherapy

Steven A. Rosenberg, James C. Yang, Richard M. Sherry, Udai S. Kammula, Marybeth S. Hughes, Giao Q. Phan, Deborah E. Citrin*, Nicholas P. Restifo, Paul F. Robbins, John R. Wunderlich, Kathleen E. Morton, Carolyn M. Laurencot, Seth M. Steinberg, Donald E. White**, and **Mark E. Dudley**

*Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD

*Radiation Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD

**Biostatistics and Data Management Section, National Cancer Institute, National Institutes of Health, Bethesda, MD

Abstract

Purpose—Most treatments for patients with metastatic melanoma have a low rate of complete regression and thus overall survival in these patients is poor. We have investigated the ability of adoptive cell transfer utilizing autologous, tumor infiltrating lymphocytes to mediate durable complete regressions in heavily pre-treated patients with metastatic melanoma.

Experimental Design—Ninety-three patients with measurable metastatic melanoma were treated with the adoptive transfer of autologous tumor-infiltrating lymphocytes administered in conjunction with interleukin-2 following a lymphodepleting preparative regimen on three sequential clinical trials. Ninety-five percent of these patients had progressive disease following a prior systemic treatment. Median potential followup was 62 months.

Results—Objective response rates by RECIST criteria in the three trials using lymphodepleting preparative regimens (chemotherapy alone or with 2Gy or 12Gy irradiation) were 49%, 52% and 72%. Twenty of the 93 patients (22%) achieved a complete tumor regression and 19 have ongoing complete regressions beyond three years The actuarial three and five year survivals for the entire group were 36% and 29% respectively but for the 20 complete responders were 100% and 93%. The likelihood of achieving a complete response was similar regardless of prior therapy. Factors associated with objective response included longer telomeres of the infused cells, the number of CD8+ CD27+ cells infused and the persistence of the infused cells in the circulation at one month (all $p_2<0.001$).

Conclusions—Cell transfer therapy with autologous tumor infiltrating can mediate durable complete responses in patients with metastatic melanoma and has similar efficacy irrespective of prior treatment.

Tumor infiltrating lymphocyte therapy for ovarian cancer and renal cell carcinoma

Rikke Andersen[1,2,*], Marco Donia[1,2], Marie Christine Wulff Westergaard[1], Magnus Pedersen[1,2], Morten Hansen[1], and Inge Marie Svane[1,2,*]

[1]Center for Cancer Immune Therapy; Department of Hematology; Herlev Hospital; Copenhagen University; Copenhagen, Denmark; [2]Department of Oncology; Herlev Hospital; Copenhagen University; Copenhagen, Denmark

Cancer Immunology, Immunotherapy
https://doi.org/10.1007/s00262-018-2174-4

ORIGINAL ARTICLE

Establishment of adoptive cell therapy with tumor infiltrating lymphocytes for non-small cell lung cancer patients

Ronny Ben-Avi[1] · Ronit Farhi[2] · Alon Ben-Nun[1] · Marina Gorodner[2] · Eyal Greenberg[2] · Gal Markel[2,3] · Jacob Schachter[2] · Orit Itzhaki[2] · Michal J. Besser[2,3]

Study of LN-145 Autologous Tumor Infiltrating Lymphocytes in the Treatment of Squamous Cell Carcinoma of the Head & Neck

STATUS: ACTIVE

Open All Close All

Description

Prospective, multicenter, single-arm, open label, interventional study evaluating adoptive cell therapy (ACT) with autologous tumor infiltrating lymphocytes (TIL) infusion (LN-145) followed by IL-2 after a non-myeloablative (NMA) lymphodepletion preparative regimen for the treatment of patients with recurrent and / or metastatic squamous cell carcinoma of the head and neck

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Call us: 1-800-4-CANCER (1-800-422-6237)

Study of LN-145, Autologous Tumor Infiltrating Lymphocytes in the Treatment of Patients With Cervical Carcinoma

STATUS: ACTIVE

Open All Close All

Description

Prospective, multicenter, single-arm, open label, interventional study evaluating adoptive cell therapy (ACT) with autologous tumor infiltrating lymphocytes (TIL) infusion (LN-145) followed by IL-2 after a non-myeloablative (NMA) lymphodepletion preparative regimen for the treatment of patients with recurrent, metastatic, or persistent cervical carcinoma

HAVE A QUESTION? WE'RE HERE TO HELP

Chat with us: LiveHelp
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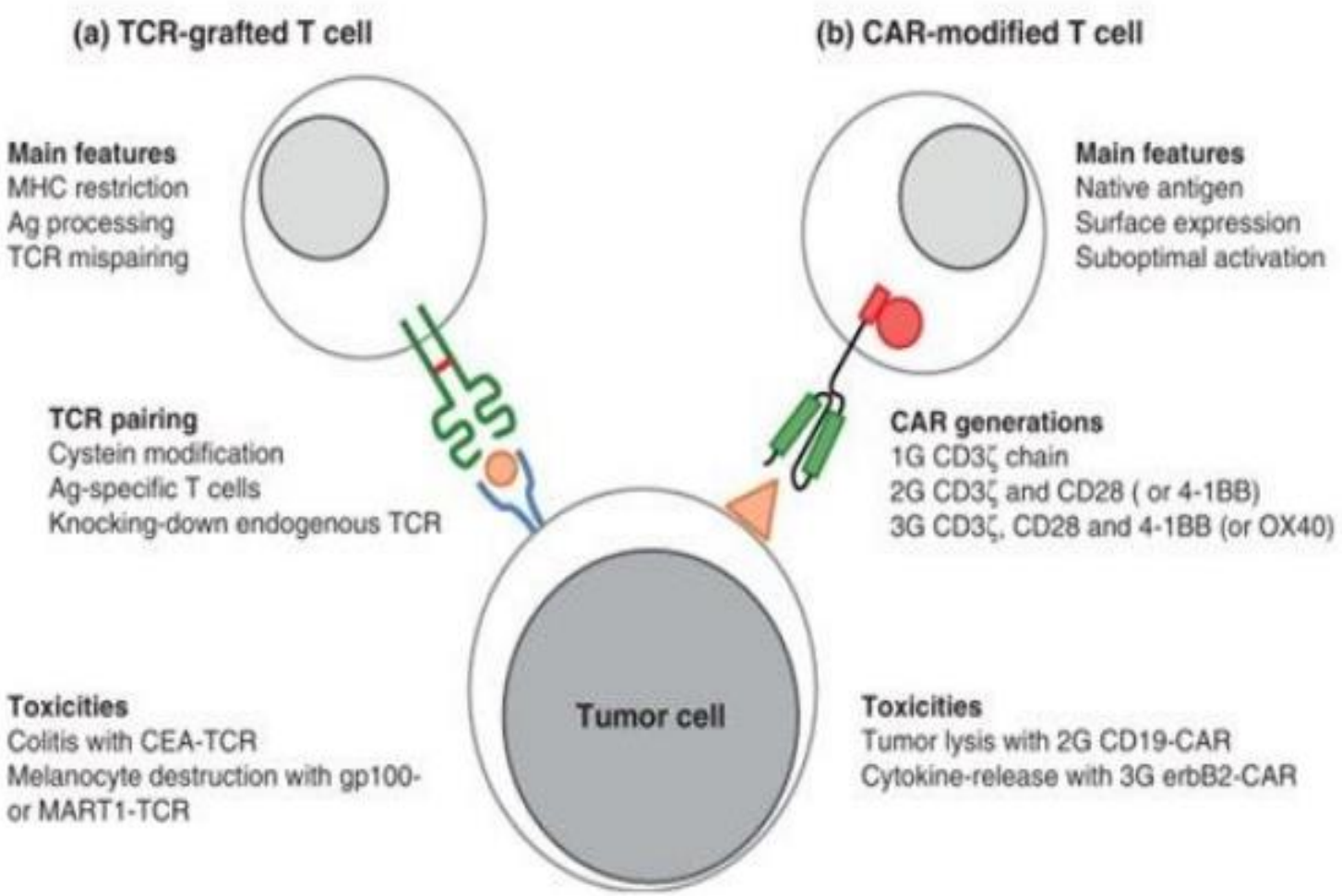
Adoptive Cell Therapy



Russo V et al Trends Mol Med. 2012

T cells expressing novel TCRs

- Modificação genética expressão de TCRs
- Isolamento células T sangue periférico
- Incorporação genes TCR no genoma
- Linfodepleção
- Reconhecimento antigénios através de MHC

T cells expressing novel TCRs

Blood
The American Society of Hematology

Gene therapy with human and mouse T-cell receptors mediates cancer regression and targets normal tissues expressing cognate antigen

Laura A. Johnson, Richard A. Morgan, [...], and Steven A. Rosenberg

JOURNAL OF CLINICAL ONCOLOGY

Tumor Regression in Patients With Metastatic Synovial Cell Sarcoma and Melanoma Using Genetically Engineered Lymphocytes Reactive With NY-ESO-1

Paul F. Robbins, Richard A. Morgan, [...], and Steven A. Rosenberg

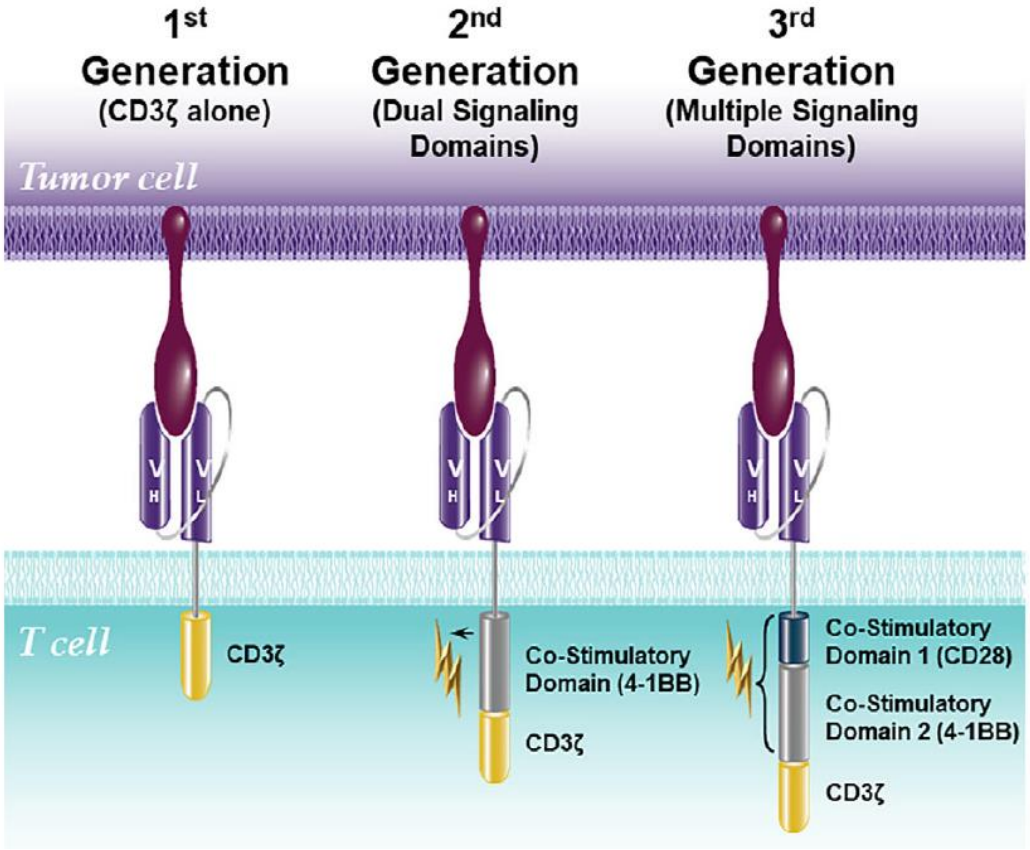
Molecular Therapy
The American Society of Gene & Cell Therapy

T Cells Targeting Carcinoembryonic Antigen Can Mediate Regression of Metastatic Colorectal Cancer but Induce Severe Transient Colitis

Maria R Parkhurst, James C Yang, [...], and Steven A Rosenberg

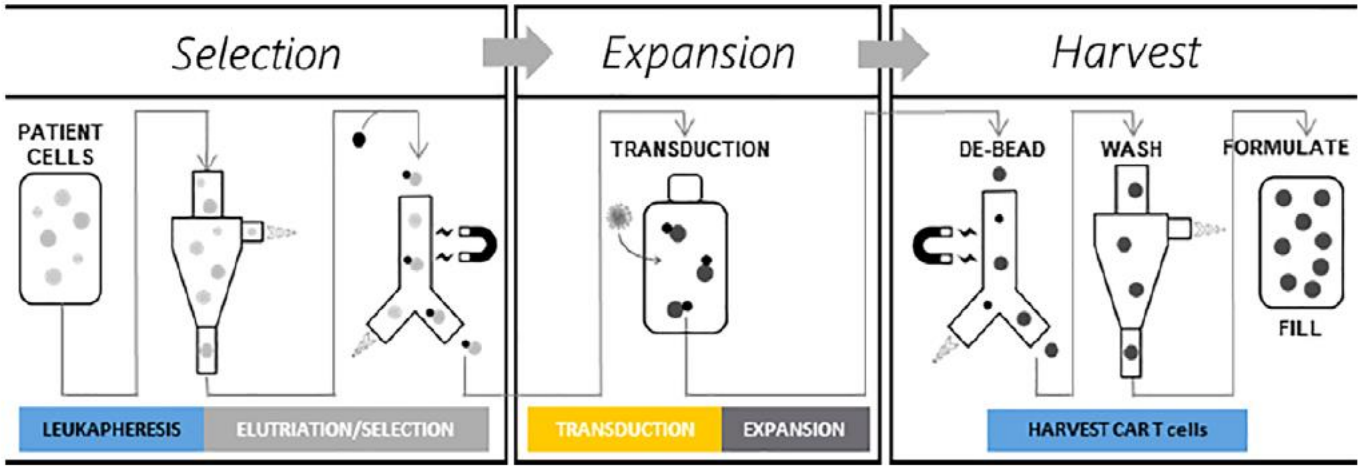
Chimeric Antigen Receptor (CAR-T cells)

- Receptores sintéticos específicos antigénios tumorais
  - Domínio extracelular: reconhecimento antigénio tumoral
  - Domínio(s) intracelular(es): indução activação células T



Feins 2019

Chimeric Antigen Receptor (CAR-T cells)



Feins 2019

Chimeric Antigen Receptor (CAR-T cells)

Published in final edited form as:

Nat Med. 2018 January ; 24(1): 20–28. doi:10.1038/nm.4441.

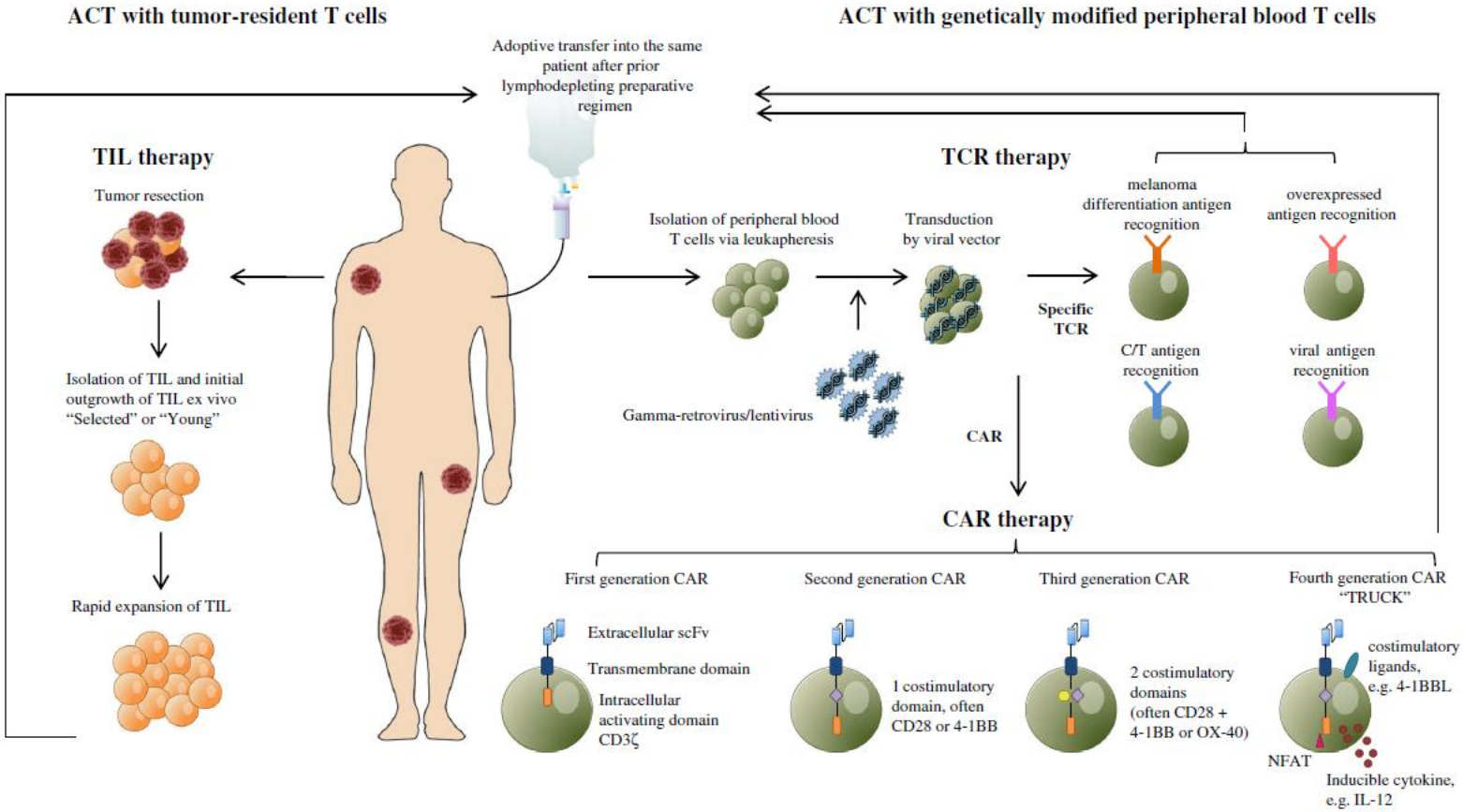
CD22-CAR T Cells Induce Remissions in CD19-CAR Naïve and Resistant B-ALL

Terry J. Fry, M.D., **Nirali N. Shah, M.D.**, **Rimas J. Orentas, Ph.D.**, **Maryalice Stetler-Stevenson, M.D., Ph.D.**, **Constance M. Yuan, M.D., Ph.D.**, **Sneha Ramakrishna, M.D.**, **Pamela Wolters, Ph.D.**, **Staci Martin, Ph.D.**, **Cindy Delbrook, R.N.**, **Bonnie Yates, P.N.P.**, **Haneen Shalabi, D.O.**, **Thomas J. Fountaine, M.D.**, **Jack F. Shern, M.D.**, **Robbie G. Majzner, M.D.**, **David F. Stroncek, M.D.**, **Marianna Sabatino, M.D.**, **Yang Feng, Ph.D.**, **Dimiter S. Dimitrov, Ph.D.**, **Ling Zhang, Ph.D.**, **Sang Nguyen**, **Haiying Qin, M.S.**, **Boro Dropulic, Ph.D.**, **Daniel W. Lee, M.D.**, and **Crystal L. Mackall, M.D.**

Pediatric Oncology Branch, (T.J.Fr., N.S., R.J.O. *, P.W., S.P-M., C.D., B.Y., H.S, T.J.Fo., J.F.S, L.Z., S.N., H.Q., S.R., P.W., S.P-M., H.O., D.W.L.,**) Cancer and Inflammation Program (Y.F., D.S.D.) and Laboratory of Pathology, (M.S.S., C.Y.), Center for Cancer Research, National Cancer Institute; Department of Transfusion Medicine, NIH Clinical Center (D.S., M.S.)- all at the National Institutes of Health, Bethesda, Maryland. Lentigen Corporation, Gaithersburg, MD (B.D. ,*),

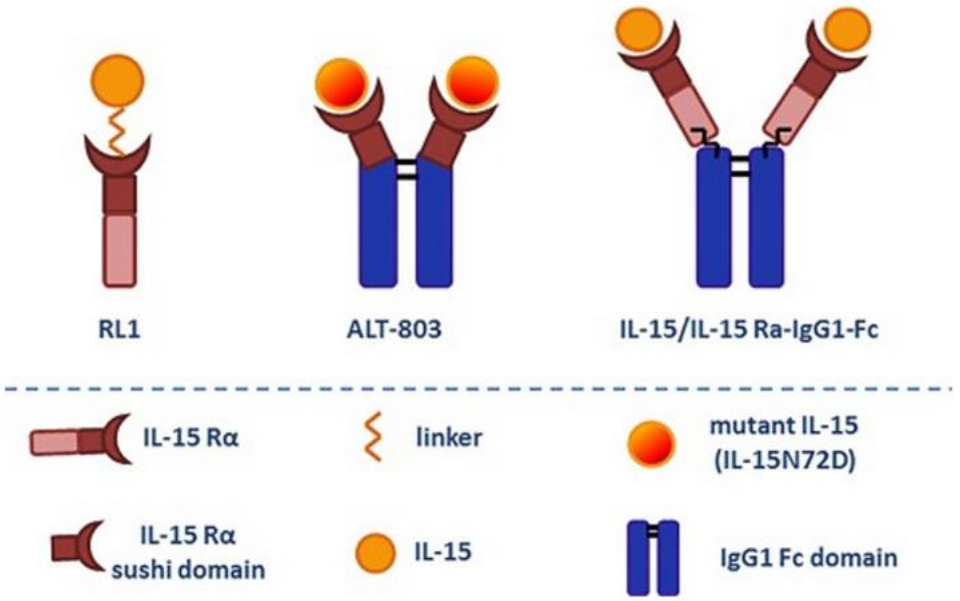
FDA NEWS RELEASE

FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma


ACT with tumor-resident T cells
ACT with genetically modified peripheral blood T cells
Adoptive transfer into the same patient after prior lymphodepleting preparative regimen
TIL therapy
Tumor resection
Isolation of TIL and initial outgrowth of TIL ex vivo "Selected" or "Young"
Rapid expansion of TIL
TCR therapy
Isolation of peripheral blood T cells via leukapheresis
Transduction by viral vector
Gamma-retrovirus/lentivirus
Specific TCR
melanoma differentiation antigen recognition
overexpressed antigen recognition
C/T antigen recognition
viral antigen recognition
CAR
CAR therapy
First generation CAR
Extracellular scFv
Transmembrane domain
Intracellular activating domain CD3ζ
Second generation CAR
1 costimulatory domain, often CD28 or 4-1BB
Third generation CAR
2 costimulatory domains (often CD28 + 4-1BB or OX-40)
Fourth generation CAR "TRUCK"
costimulatory ligands, e.g. 4-1BBL
NFAT
Inducible cytokine, e.g. IL-12

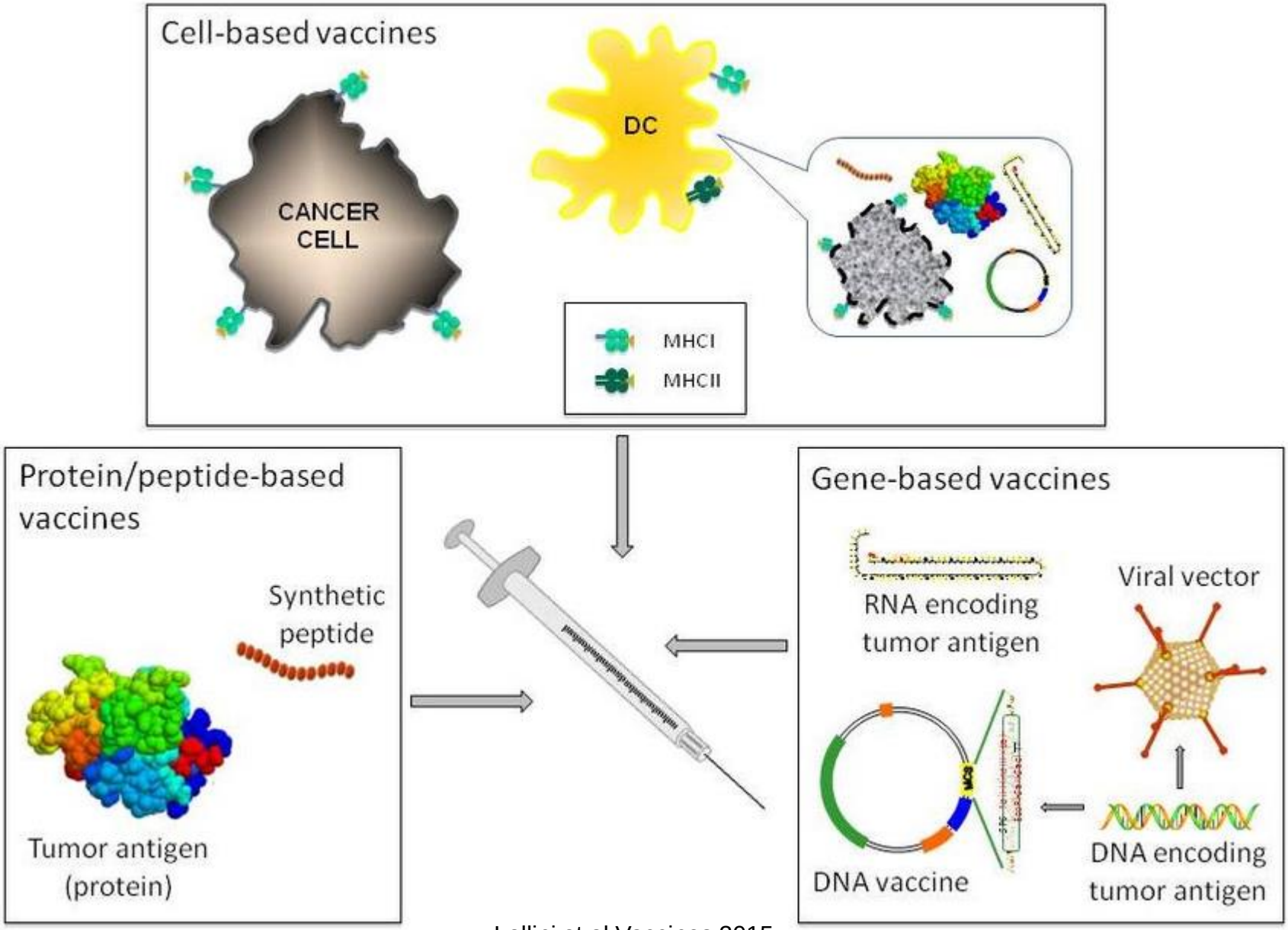
Citoquinas

- Proliferação e activação de células T efectoras
- Apoptose e inibição da proliferação de células tumorais
- IL-2: carcinoma renal metastático e melanoma metastático



American Society of Clinical Oncology 2018

Vacinas



Lollini et al Vaccines 2015

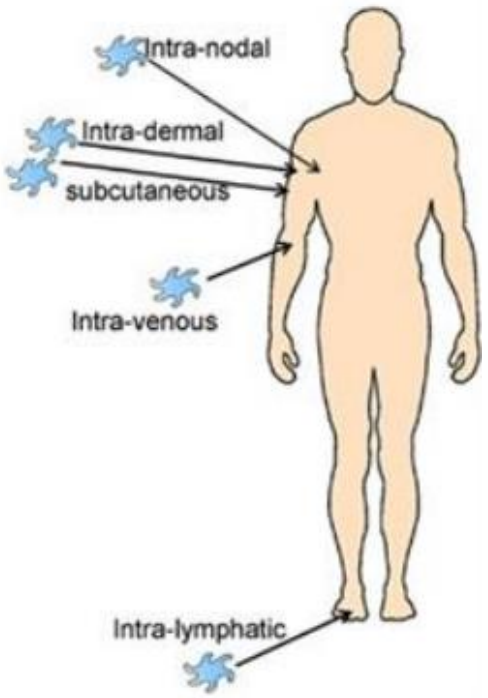
Vacinas

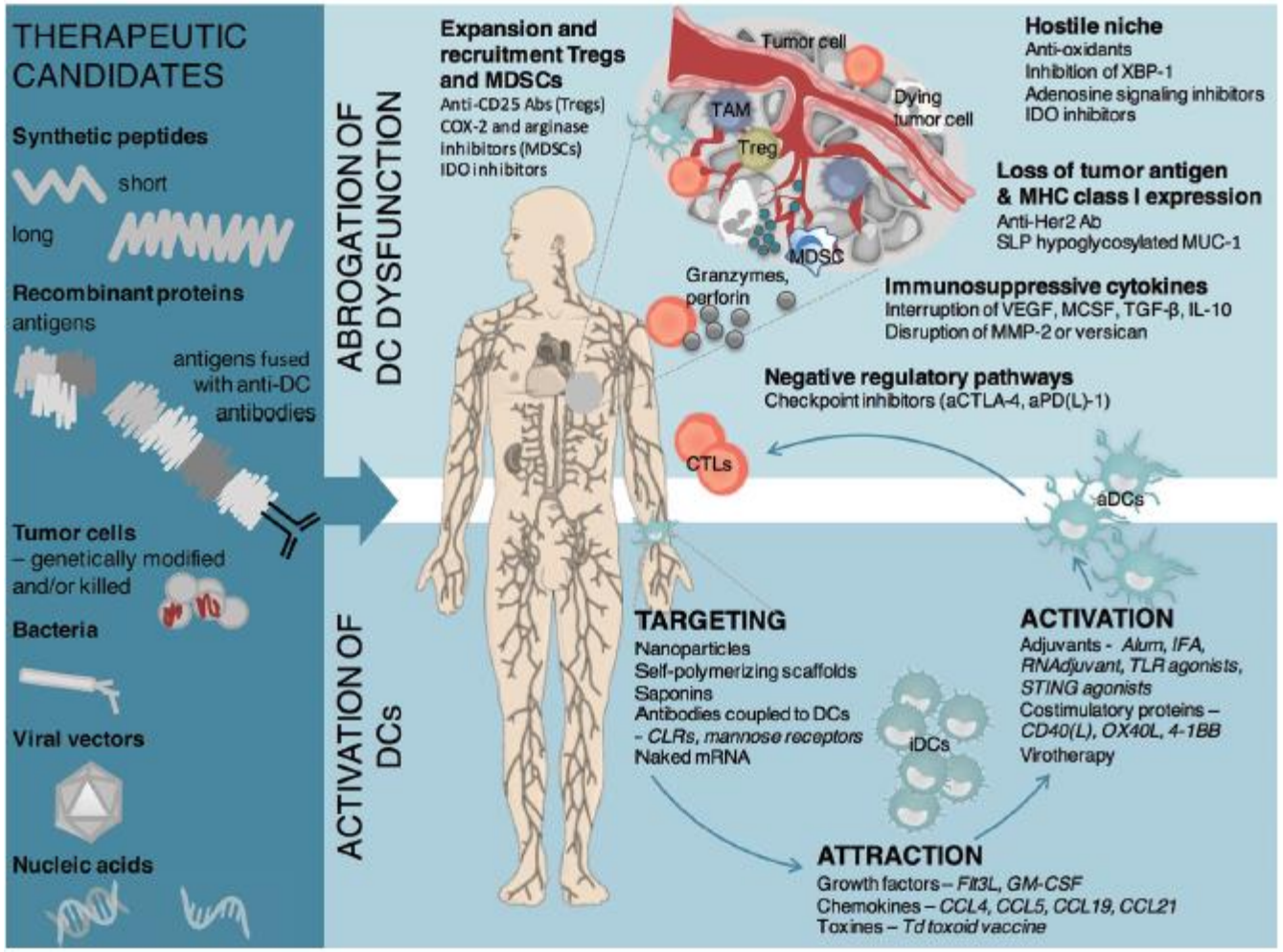
- Requerimentos:
  - Antigénio internalizado pelas CD
  - Adjuvante não-específico
    - Citoquinas
    - Proteínas inflamatórias
    - CD
    - Citoquinas produzidas por CD

Vacinas com células dendríticas

Vacinação ex vivo

1. Isolamento
2. Tumor associated antigens (TAAs)
3. Estímulos maturação
4. Reintrodução



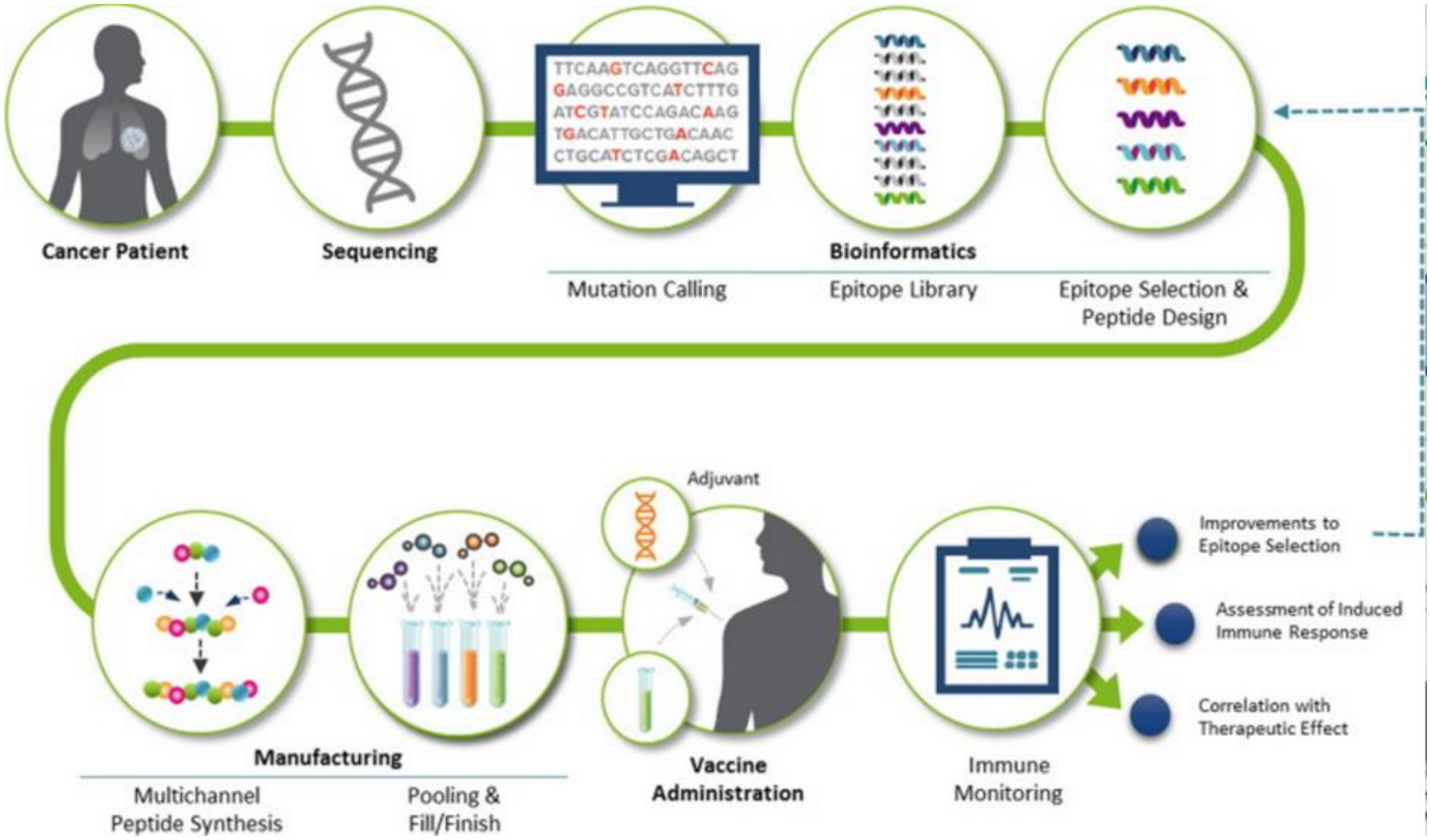

THERAPEUTIC CANDIDATES
Synthetic peptides
short
long
Recombinant proteins
antigens
antigens fused with anti-DC antibodies
Tumor cells
– genetically modified and/or killed
Bacteria
Viral vectors
Nucleic acids
ABROGATION OF DC DYSFUNCTION
Expansion and recruitment Tregs and MDSCs
Anti-CD25 Abs (Tregs)
COX-2 and arginase inhibitors (MDSCs)
IDO inhibitors
Tumor cell
TAM
Treg
Dying tumor cell
MDSC
Hostile niche
Anti-oxidants
Inhibition of XBP-1
Adenosine signaling inhibitors
IDO inhibitors
Loss of tumor antigen & MHC class I expression
Anti-Her2 Ab
SLP hypoglycosylated MUC-1
Granzymes, perforin
Immunosuppressive cytokines
Interruption of VEGF, MCSF, TGF-β, IL-10
Disruption of MMP-2 or versican
Negative regulatory pathways
Checkpoint inhibitors (aCTLA-4, aPD(L)-1)
CTLs
aDCs
ACTIVATION OF DCs
TARGETING
Nanoparticles
Self-polymerizing scaffolds
Saponins
Antibodies coupled to DCs
- CLRs, mannose receptors
Naked mRNA
iDCs
ACTIVATION
Adjuvants - Alum, IFA, RNAdjuvant, TLR agonists, STING agonists
Costimulatory proteins – CD40(L), OX40L, 4-1BB
Virotherapy
ATTRACTION
Growth factors – Flt3L, GM-CSF
Chemokines – CCL4, CCL5, CCL19, CCL21
Toxines – Td toxoid vaccine

Vacinas com células dendríticas

Vacinação in situ

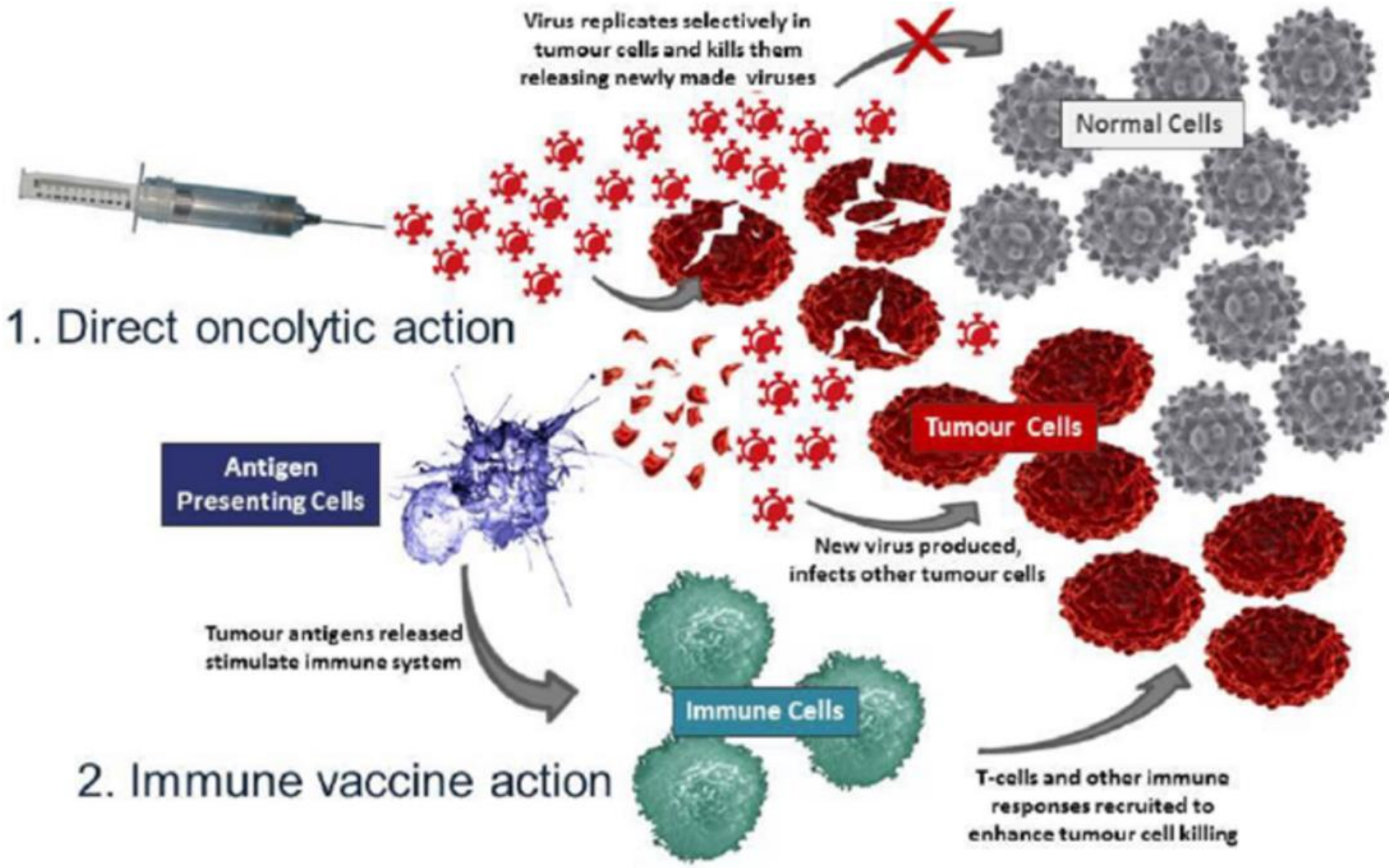
1. Atracção
2. Activação
    - sais de alumínio
    - IFA
    - RNAdjuvant
    - agonistas TLR
    - viroterapia
3. Entrega
    - nanopartículas, anticorpos, mRNA

Vacinas personalizadas com neoantigénios



American Society of Clinical Oncology 2018

Vacinas oncolíticas



JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Talimogene Laherparepvec Improves Durable Response Rate in Patients With Advanced Melanoma

Robert H.I. Andtbacka, Howard L. Kaufman, Frances Collichio, Thomas Amatruda, Neil Senzer, Jason Chesney, Keith A. Delman, Lynn E. Spitler, Igor Puzanov, Sanjiv S. Agarwala, Mohammed Milhem, Lee Cranmer, Brendan Curti, Karl Lewis, Merrick Ross, Troy Guthrie, Gerald P. Linette, Gregory A. Daniels, Kevin Harrington, Mark R. Middleton, Wilson H. Miller Jr, Jonathan S. Zager, Yining Ye, Bin Yao, Ai Li, Susan Doleman, Ari VanderWalde, Jennifer Gansert, and Robert S. Coffin

See accompanying article on page 2812

Author affiliations appear at the end of this article.

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R.H.I.A. and H.L.K. contributed equally to this work.

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Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

Clinical trial information: NCT00769704.

Corresponding author: Howard L. Kaufman, MD, FACS, Rutgers Cancer Institute of New Jersey, 195 Little Albany St, New Brunswick, NJ 08901; e-mail: howard.kaufman@rutgers.edu.

0732-183X/15/3325w-2780w/$20.00

DOI: 10.1200/JCO.2014.58.3377

ABSTRACT

Purpose
Talimogene laherparepvec (T-VEC) is a herpes simplex virus type 1–derived oncolytic immunotherapy designed to selectively replicate within tumors and produce granulocyte macrophage colony-stimulating factor (GM-CSF) to enhance systemic antitumor immune responses. T-VEC was compared with GM-CSF in patients with unresected stage IIIB to IV melanoma in a randomized open-label phase III trial.

Patients and Methods
Patients with injectable melanoma that was not surgically resectable were randomly assigned at a two-to-one ratio to intralesional T-VEC or subcutaneous GM-CSF. The primary end point was durable response rate (DRR; objective response lasting continuously ≥ 6 months) per independent assessment. Key secondary end points included overall survival (OS) and overall response rate.

Results
Among 436 patients randomly assigned, DRR was significantly higher with T-VEC (16.3%; 95% CI, 12.1% to 20.5%) than GM-CSF (2.1%; 95% CI, 0% to 4.5%]; odds ratio, 8.9; $P < .001$). Overall response rate was also higher in the T-VEC arm (26.4%; 95% CI, 21.4% to 31.5% *v* 5.7%; 95% CI, 1.9% to 9.5%). Median OS was 23.3 months (95% CI, 19.5 to 29.6 months) with T-VEC and 18.9 months (95% CI, 16.0 to 23.7 months) with GM-CSF (hazard ratio, 0.79; 95% CI, 0.62 to 1.00; $P = .051$). T-VEC efficacy was most pronounced in patients with stage IIIB, IIIC, or IVM1a disease and in patients with treatment-naive disease. The most common adverse events (AEs) with T-VEC were fatigue, chills, and pyrexia. The only grade 3 or 4 AE occurring in ≥ 2% of T-VEC–treated patients was cellulitis (2.1%). No fatal treatment-related AEs occurred.

Conclusion
T-VEC is the first oncolytic immunotherapy to demonstrate therapeutic benefit against melanoma in a phase III clinical trial. T-VEC was well tolerated and resulted in a higher DRR ($P < .001$) and longer median OS ($P = .051$), particularly in untreated patients or those with stage IIIB, IIIC, or IVM1a disease. T-VEC represents a novel potential therapy for patients with metastatic melanoma.

J Clin Oncol 33:2780-2788. © 2015 by American Society of Clinical Oncology

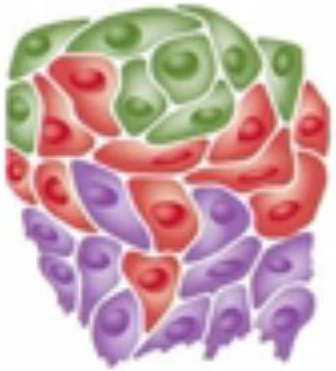
Monitorização do sistema imunitário

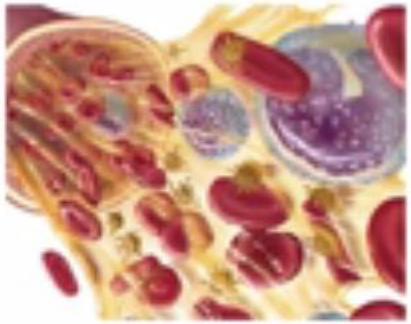
1. **Exames baseados em Sangue**

2. **Exame baseados Tumor/Tecido**

Monitorização do sistema imunitário

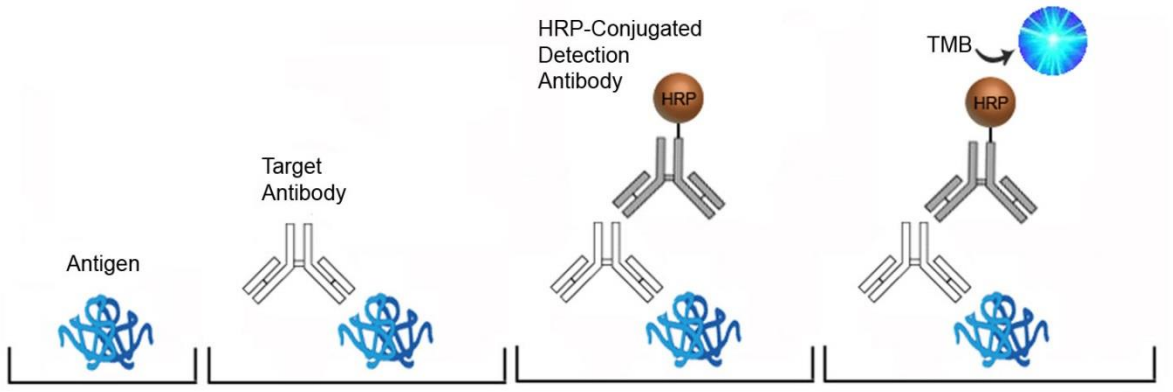
Tumor tissue	Peripheral blood
At the site of the action	Assumed reflective of tumor
Sometime difficult or impossible to obtain	Easy to obtain
Very limited quantity	Flexible quantity
Limits ability to evaluate immunity over time	Amenable to multiple time point monitoring
Tumor heterogeneity	Systemic-less heterogeneic?



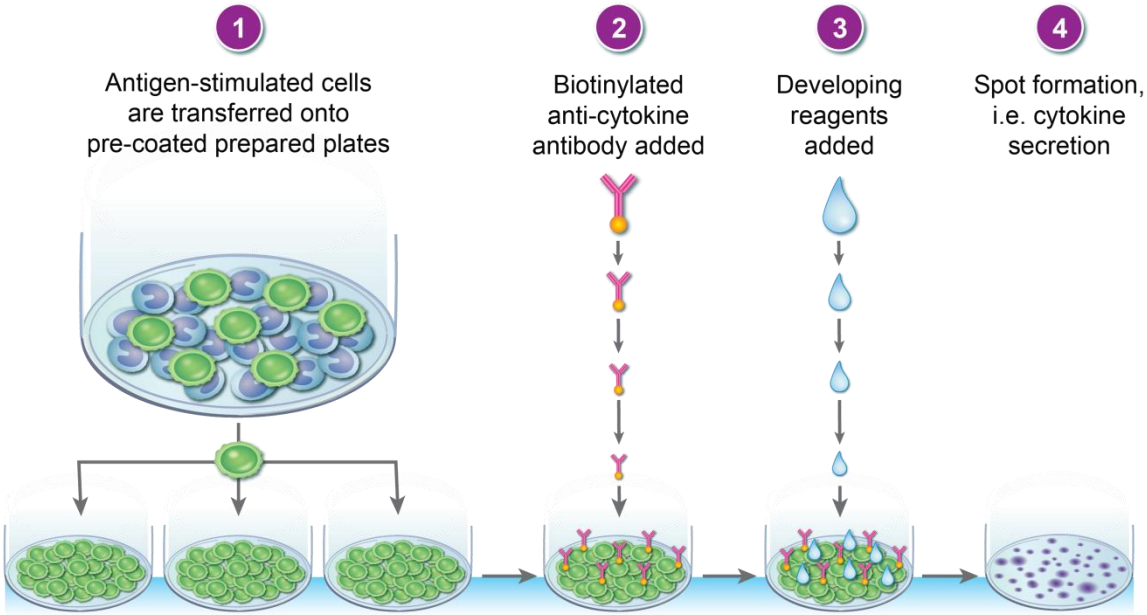


Sangue periférico

- **ELISA**

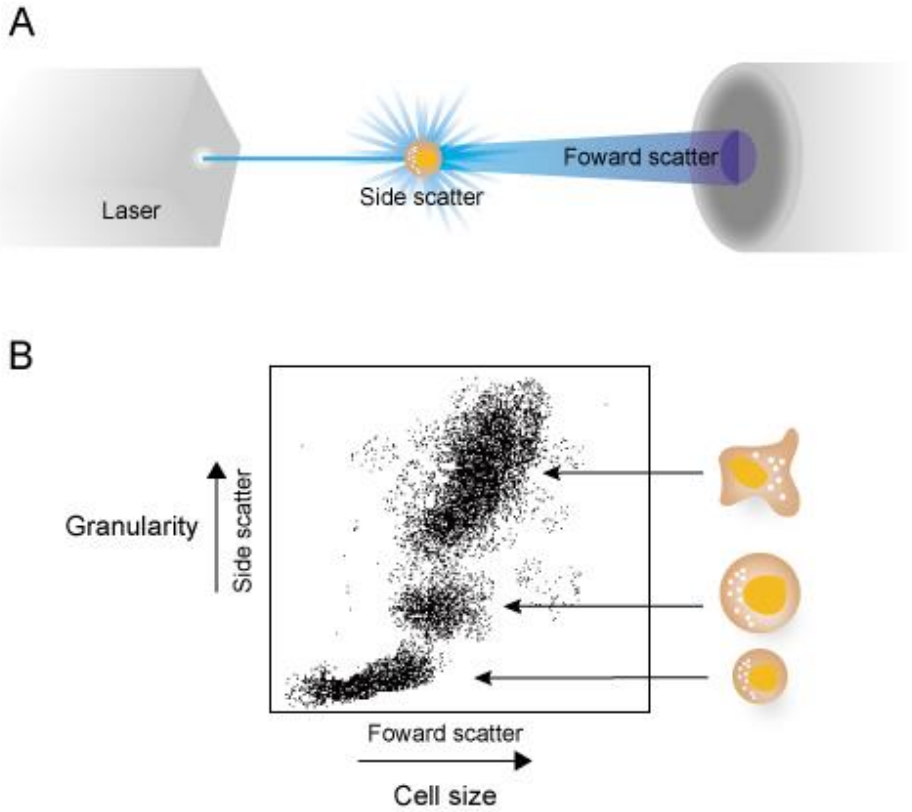


- **ELISPOT**



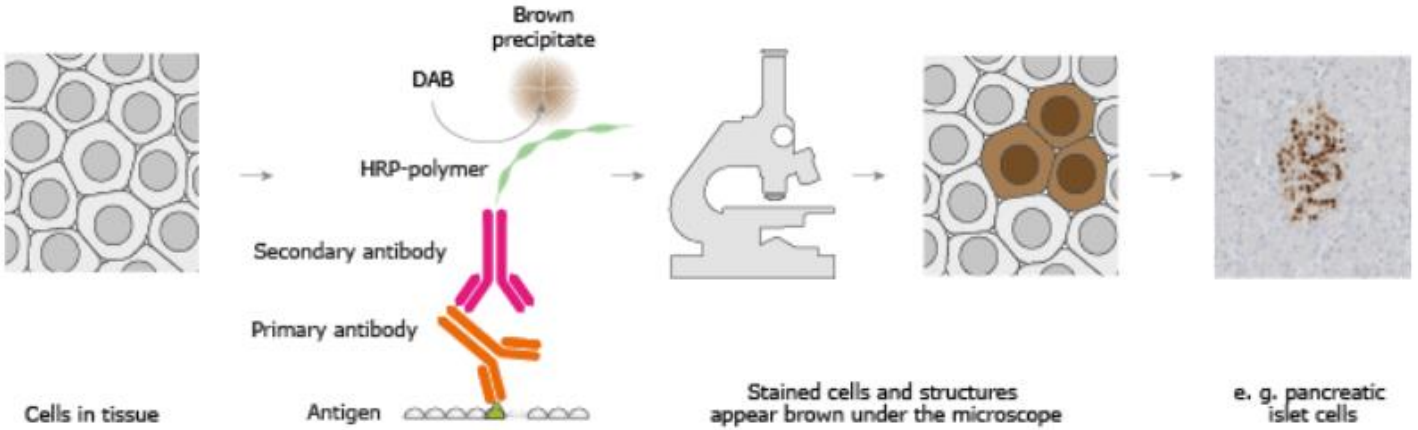
Sangue periférico

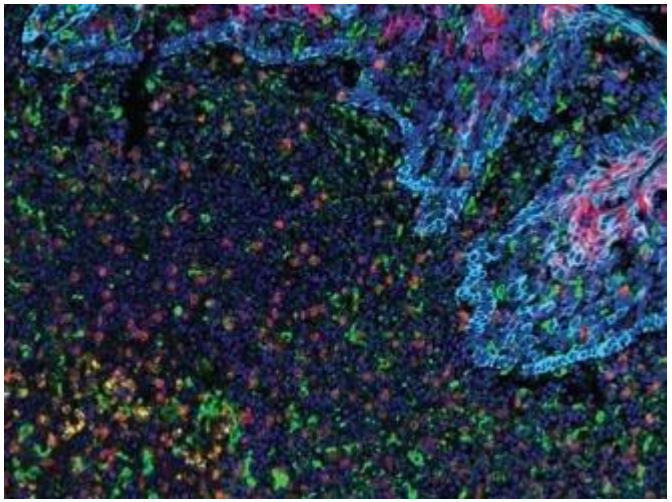
- **Citometria Fluxo**



Tumor

- **Imunohistoquímica**

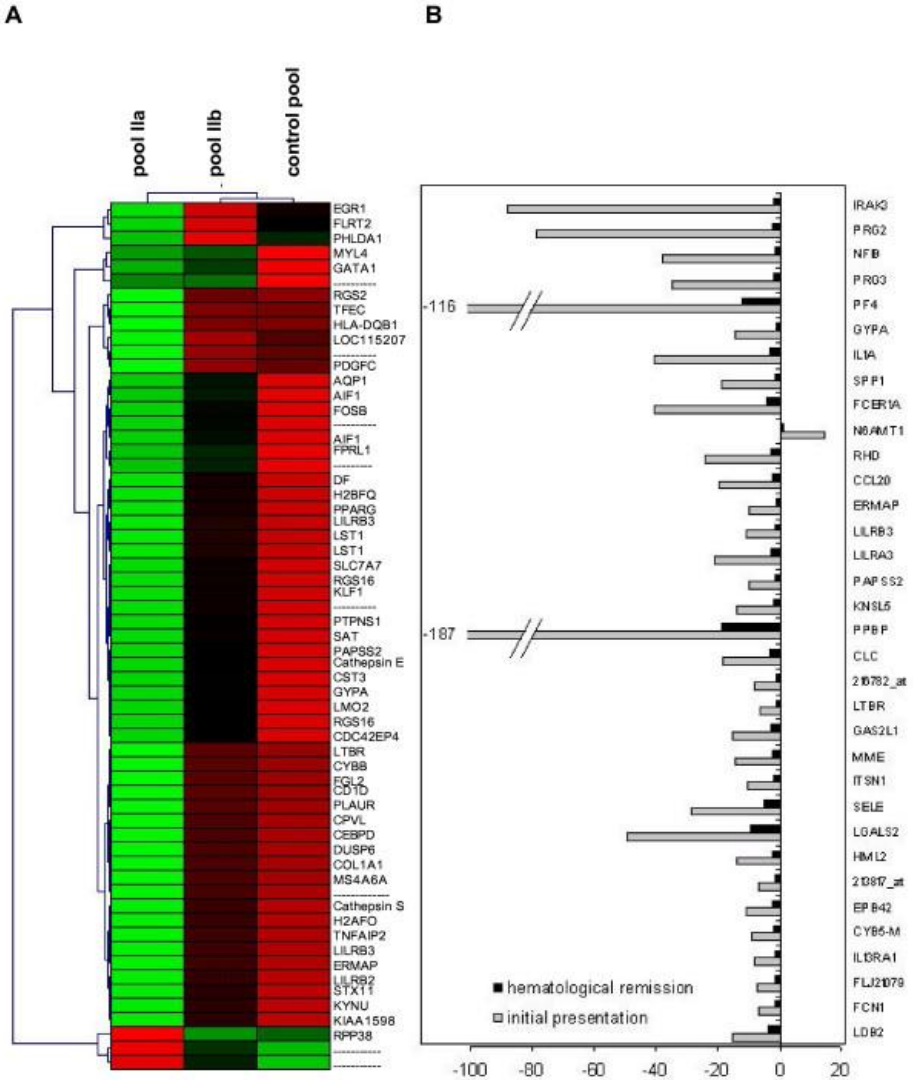




Tumor

- **Gene expression analysis**

- **Análise mutacional**



Franke et al BMC Genomics 2006

Workshop Imunoterapia

Ana Ramos Coelho, Ph.D.

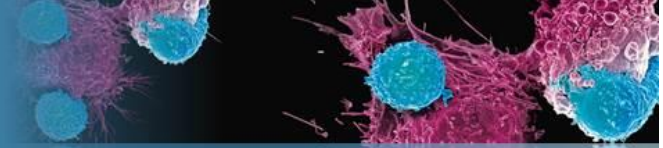
[1] Escola Superior de Tecnologia da Saúde de Lisboa, ESTeSL, Instituto Politécnico de Lisboa, Av. D. João II, Lote 4.69.01, 1990-096 Lisboa, Portugal, ana.ramos@estesl.ipl.pt

[2] H&TRC - Centro de Investigação em Saúde e Tecnologia

III Congresso Nacional em Ciências Biomédicas Laboratoriais

25 outubro de 2019

ESCOLA SUPERIOR DE TECNOLOGIA DA SAÚDE DE LISBOA
INSTITUTO POLITÉCNICO DE LISBOA



Pós-Graduação em
Avanços em Oncobiologia molecular aplicada ao diagnóstico e terapêutica

DESTINATÁRIOS

Profissionais de saúde, Investigadores e Professores das ciências biológicas e das ciências da saúde.

MÓDULOS

1. Fundamentos em oncobiologia
2. Metodologias de Patologia Molecular aplicadas à clínica
3. Pesquisa de variantes de DNA
4. Perfil molecular e biomarcadores oncológicos
5. Biópsia líquida e DNA tumoral circulante: aplicações em oncobiologia
6. Imunoterapia
7. Tecnologia CRISPR: aplicações terapêuticas
8. Oncologia integrada

OBJETIVOS

- Compreender o processo de transformação, progressão, metastização tumoral e oncogénese microbiana.
- Conhecer as vias de sinalização implicadas na tumorigénese.
- Conhecer os tipos de cancros, respetivo diagnóstico e princípios major de tratamento.
- Conhecer a tecnologia CRISPR e respetivas aplicações terapêuticas.
- Compreender a importância da imunoterapia e conhecer a sua importância clínica.
- Conhecer o perfil molecular e biomarcadores dos cancros mais comuns.
- Conhecer e compreender as aplicações da biópsia líquida no âmbito da oncobiologia.
- Conhecer e dominar a análise de ácidos nucleicos circulantes no âmbito da oncobiologia.
- Conhecer as *guidelines* práticas do *Next Generation Sequencing* (NGS) em oncologia.
- Compreender as *guidelines* para a classificação, interpretação e elaboração de relatórios de variantes genéticas.
- Realizar a análise e controlo de qualidade de dados de NGS, para a deteção de SNPs.
- Conhecer e compreender as técnicas mais recentes de Patologia Molecular aplicadas à clínica.

DURAÇÃO | ECTS

106 horas | 17 ECTS

FORMADORES

Ana Ramos Coelho, ESTeSL-IPL
Miguel Brito, ESTeSL-IPL
Mário Matos, ESTeSL-IPL
Ana Almeida, ESTeSL-IPL
Maria Sofia Quental, IPATIMUP
Marta Barbosa, Hospital do Espírito Santo
Joana Vaz, Germano de Sousa
Joana Caldeira, i3S/INEB
Anita Gomes, ESTeSL-IPL
Karine Serre, IMM
André Coelho, ESTeSL-IPL
Carina Silva, ESTeSL-IPL
Amadeu Ferro, ESTeSL-IPL
Alexandre Salvador, Enzifarma
Sónia Matos, Genomed

Saiba aqui mais sobre os Formadores

AGENDA

Quinta e sexta-feira, 18h00 às 22h00
Sábado, 9h30 às 18h00
Início: 7 novembro 2019
Fim: 11 janeiro 2020

CRITÉRIOS DE SERIAÇÃO

- Ordem de inscrição

VALOR

450€ | 350€*
Nota: Modalidades de pagamento – De uma só vez ou em três prestações:
1ª prestação – em 1 de novembro 2019 – 150€ | 120€*
2ª prestação – em 1 de dezembro 2019 – 150€ | 120€*
3ª prestação – em 1 de janeiro 2020 – 150€ | 110€*

Taxa de Candidatura: 15€

Pode ainda ser realizada por Módulos
(inscrição máxima em 6 módulos):
- Módulo 3,4,5,6,8 – 80€ | 50€*
- Módulo 1,2 e 7 – 50€ | 40€*

* Docentes e Orientadores de Estágio da ESTeSL 2019/2020, membros da Associação AlumniESTeSL e antigos alunos.

NÚMERO DE VAGAS | 30

Nº mínimo para o funcionamento da pós-graduação: 15
Nº mínimo para o funcionamento dos módulos: 10

INFORMAÇÕES

www.estesl.ipl.pt
formacaocontinua@estesl.ipl.pt
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ScienceWithArt

November 11th, 6.30 p.m. I Amphitheatre

Medicines and dietary supplements in performance consumptions: social practices, contexts and literacy

David Tavares, Ph.D. ESTeSL-IPL, H&TRC, CIES-IUL

Host: Nuno Medeiros, Ph.D. ESTeSL-IPL, H&TRC

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