



Eliane Piaggio  
PhD, DR2 INSERM, Chef d'équipe  
eliane.piaggio@curie.fr  
Tel: +33 1 56 24 58 05

## **Cancer immunotherapy can be viewed as “The Breakthrough of 2013”, switching cancer treatment from targeting the tumor to targeting the immune system.**

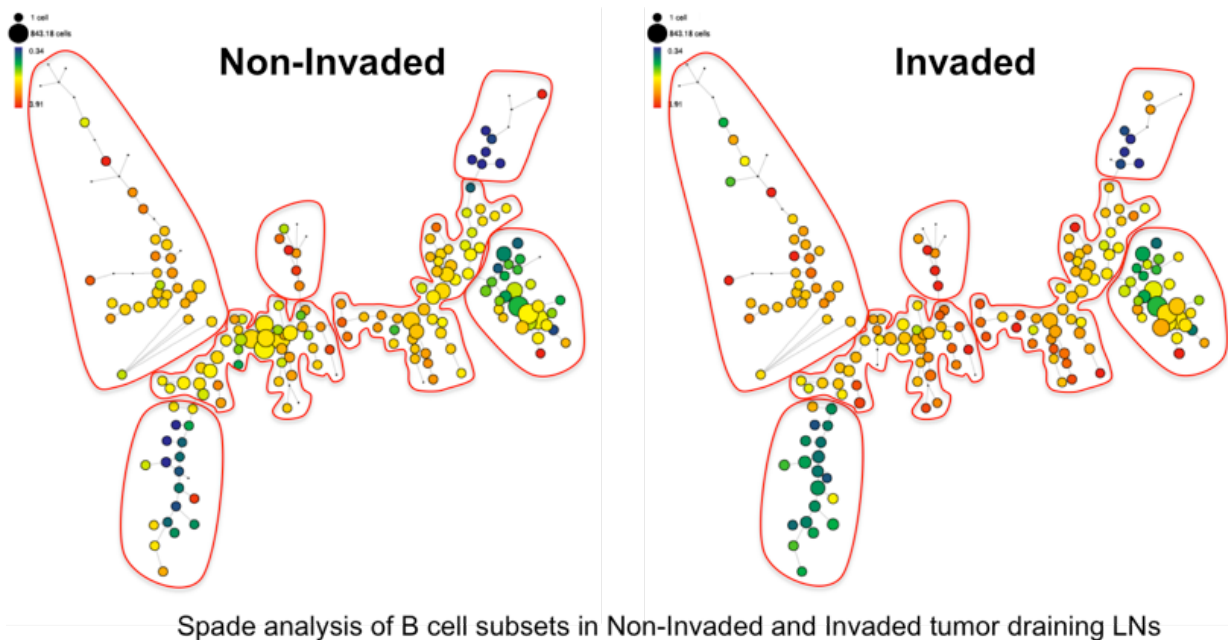
The blockade of immune checkpoints with antibodies (Ab) anti-CTLA-4, anti-PD1 and anti-PD-L1, has given impressive clinical results and manageable safety profiles. As reports of therapeutic efficacy with checkpoint inhibitors extend from metastatic melanoma, renal cell carcinoma and lung cancer to other tumors, **the opportunity arises for other type of cancer patients, including breast, ovarian, head & neck (H&N), and paediatric tumours to benefit from these new therapies.** There is no doubt that in the upcoming years, immunotherapy will represent a substantial part of the therapeutic arsenal to treat cancer.

### **3- Our main research programs and achievements:**

#### **a. Immunotherapy studies based on the analysis of human tumor-draining lymph nodes (LNs).**

We are performing a holistic comparison of the immune profile of invaded versus non-invaded LNs. Our aim is to identify immunomodulatory mechanisms associated to the presence of the invading tumor in the LNs, and to discover biomarkers that could guide the design of patient-tailored immune therapies. Techniques: phenotypic and functional analysis of tumor, fibroblasts, B and T, DCs and NK cells by multi-parametric flow cytometry, ELISPOT, LUMINEX, RNAseq, phage display.... We have established national and international collaborations with groups expert in each of the subpopulation studied. We have created a lymph node collection for research purposes.

One special focus is the study of tumor neoepitopes for future personalized anti-cancer vaccines.

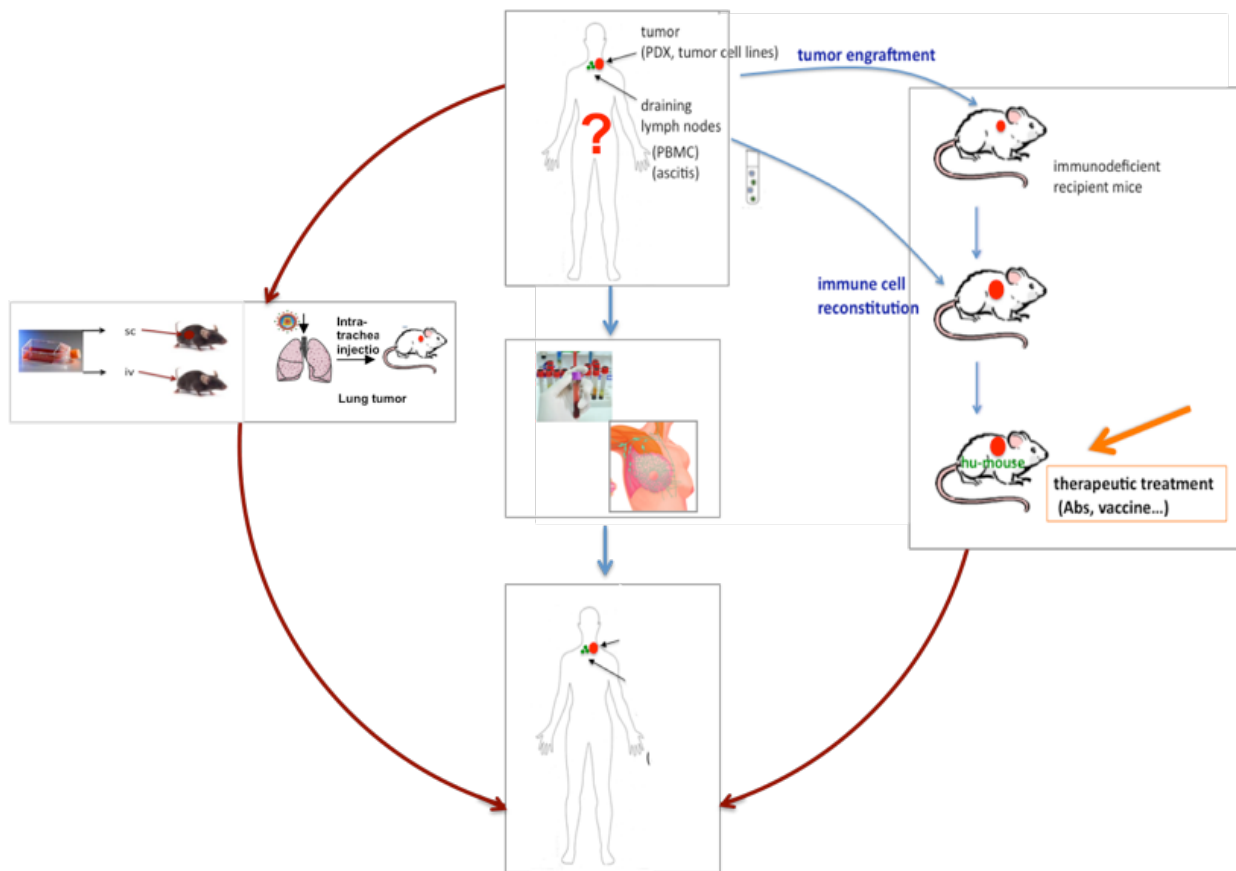


### b. Translation of IL-2/anti-IL-2 Ab complexes immunotherapy to the clinics

The FDA has already approved high-dose IL-2 therapy for metastatic melanoma and renal carcinoma treatment. However, high-dose of IL-2 administration is highly toxic and has low efficacy. In this project, we want to use IL-2/anti-IL-2 complexes directed to CD8+ and NK T cells, in view of clinical application, as monotherapy or combined with other immunotherapies in different tumor mouse models.

### c. Study immunotherapies in optimized in vivo models for cancer

To improve our understanding and to build better and more translatable in vivo mouse tumor models, we are developing humanized mouse models consisting of the transplant of patient-derived tumor xenografts into immunodeficient mice reconstituted with human immune cells (isolated from the matching patient from the draining LNs or with allogenic PBMCs or LN cells). This is a collaborative project with the Laboratory of Preclinical Investigation, LIP. The final aim is improving therapeutic effect and defining rationalized drug combinations with immune checkpoints and proprietary molecules developed by collaborators, including novel immunomodulatory approaches generated at our unit. Also, using this model we are evaluating the role of microbiota on the response to anti-PD-1 Ab treatment.



## Key publications

### Year of publication 2020

Pierre Bourdely, Giorgio Anselmi, Kristine Vaivode, Rodrigo Nalio Ramos, Yoann Missolo-Koussou, Sofia Hidalgo, Jimena Tosselo, Nicolas Nuñez, Wilfrid Richer, Anne Vincent-Salomon, Alka Saxena, Kristie Wood, Alvaro Lladser, Eliane Piaggio, Julie Helft, Pierre Guermonprez (2020 Jul 2) **Transcriptional and Functional Analysis of CD1c Human Dendritic Cells Identifies a CD163 Subset Priming CD8CD103 T Cells.**

*Immunity* : 335-352.e8 : [DOI : S1074-7613\(20\)30232-6](https://doi.org/10.1016/j.immuni.2020.07.006)

Nicolas Gonzalo Núñez, Jimena Tosello Boari, Rodrigo Nalio Ramos, Wilfrid Richer, Nicolas Cagnard, Cyrill Dimitri Anderfuhren, Leticia Laura Niborski, Jeremy Bigot, Didier Meseure, Philippe De La Rochere, Maud Milder, Sophie Viel, Delphine Loirat, Louis Pérol, Anne Vincent-Salomon, Xavier Sastre-Garau, Becher Burkhard, Christine Sedlik, Olivier Lantz, Sebastian Amigorena, Eliane Piaggio (2020 Jul 1)

**Tumor invasion in draining lymph nodes is associated with Treg accumulation in breast cancer patients.**

*Nature communications* : 3272 : [DOI : 10.1038/s41467-020-17046-2](https://doi.org/10.1038/s41467-020-17046-2)

**Year of publication 2017**

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Fernando P Canale, Maria C Ramello, Nicolas Núñez, Cintia L Araujo Furlan, Sabrina N Bossio, Melisa Gorosito Serrán, Jimena Tosello Boari, Andrés Del Castillo, Marta Ledesma, Christine Sedlik, Eliane Piaggio, Adriana Gruppi, Eva V Acosta Rodríguez, Carolina L Montes (2017 Oct 26)  
**CD39 expression defines cell exhaustion in tumor-infiltrating CD8+ T cells.**

*Cancer research* : [DOI : canres.2684.2016](https://doi.org/10.1158/1538-7443.2017.2684)

Rodrigo N Ramos, Eliane Piaggio, Emanuela Romano (2017 Mar 19)

**Mechanisms of Resistance to Immune Checkpoint Antibodies.**

*Handbook of experimental pharmacology* : [DOI : 10.1007/164\\_2017\\_11](https://doi.org/10.1007/164_2017_11)

**Year of publication 2016**

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Louis Pérol, John M Lindner, Pamela Caudana, Nicolas Gonzalo Nunez, Audrey Baeyens, Andrea Valle, Christine Sedlik, Delphine Loirat, Olivier Boyer, Alain Créange, José Laurent Cohen, Ute Christine Rogner, Jun Yamanouchi, Martine Marchant, Xavier Charles Leber, Meike Scharenberg, Marie-Claude Gagnerault, Roberto Mallone, Manuela Battaglia, Pere Santamaria, Agnès Hartemann, Elisabetta Traggiai, Eliane Piaggio (2016 Oct 7)

**Loss of immune tolerance to IL-2 in type 1 diabetes.**

*Nature communications* : 13027 : [DOI : 10.1038/ncomms13027](https://doi.org/10.1038/ncomms13027)

**Year of publication 2015**

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Louis Pérol, Eliane Piaggio (2015 Nov 5)

**New Molecular and Cellular Mechanisms of Tolerance: Tolerogenic Actions of IL-2.**

*Methods in molecular biology (Clifton, N.J.)* : 11-28 : [DOI : 10.1007/978-1-4939-3139-2\\_2](https://doi.org/10.1007/978-1-4939-3139-2_2)