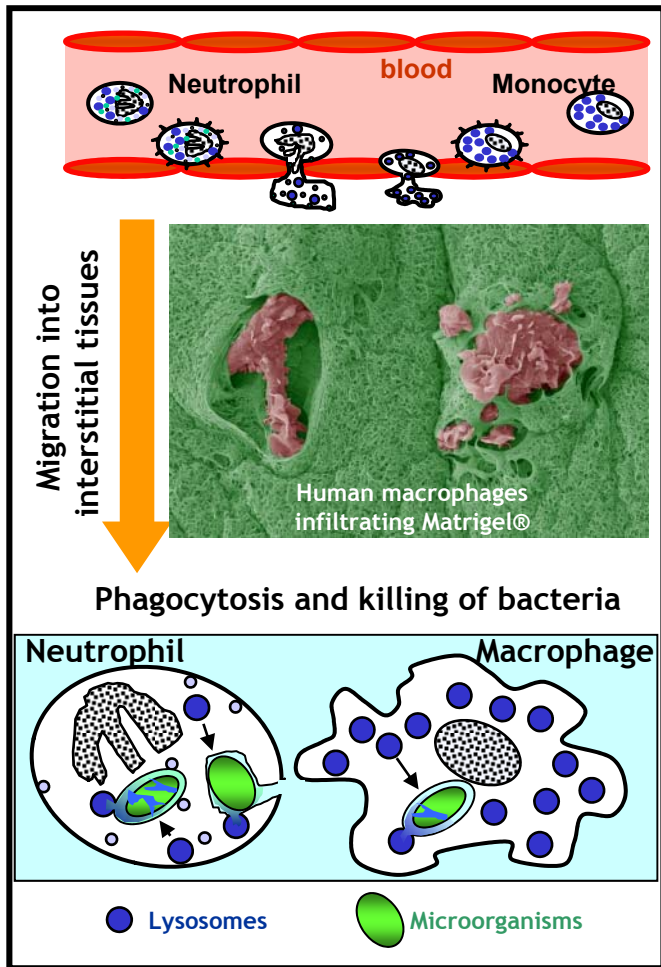


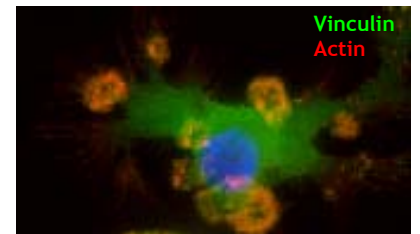
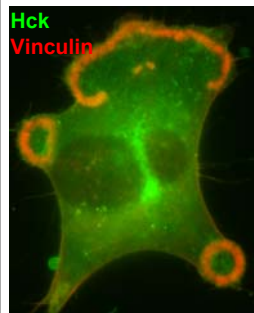
Differentiation and Activation of Phagocytes

Group Leader : Isabelle Maridonneau-Parini



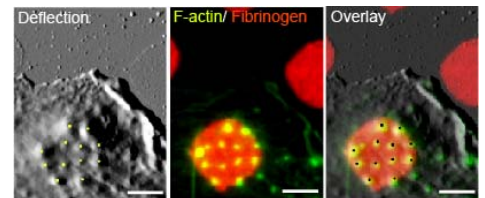
Research program. Identification of the molecular and cellular mechanisms controlling the 3D migration of phagocytes : role of the tyrosine kinase Hck ; structure and dynamics of podosomes ; mobilisation of lysosomes.

Perspectives: identification of pharmacological targets controlling phagocyte 3D migration



Podosome rosettes in human macrophage.

Podosome rosettes induced by Hck : active Hck was ectopically expressed in mouse fibroblasts and induced the formation of rosettes of podosomes, adherence structures involved in extra-cellular matrix degradation.



Correlative microscopy: AFM imaging (grey) of a human macrophage grown on micro-patterned fibrinogen (red) that locally induced the biogenesis of podosomes (green). Bar = 4 μ m

Collaborations : CA Lowell (San Francisco, USA), E. Biessen (Lieden, N), E. Genot (Bordeaux), P. Jurdic (Lyon), S. Benichou, F. Niedergang, P. Chavrier (Paris), C. Vieu, A. Valette (Toulouse)

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Team : **Permanents :** I. Maridonneau-Parini (DR2 INSERM), V. Le Cabec (CR1 CNRS), C. Cougoule (CR2 CNRS), A. Labrousse (MCU). **Post-doctoral fellows :** C. V  rollet, G. Charri  re. **PhD students :** R. Guiet (3rd year), E. van Goethem (3rd year), A. Labernadie (2nd year), W. Aslam (3rd year). **M2R :** J. Record

Significant Publications :

- Van Goethem E, Poincloux R, Gauffre F, Maridonneau-Parini I, Le Cabec V. (2010) Matrix architecture dictates three-dimensional migration modes of human macrophages: differential involvement of proteases and podosome-like structures. *J Immunol.* 184,1049-61
- Cougoule C, Le Cabec V, Poincloux R, Al Saati T, Mege JL, Tabouret G, Lowell CA, Laviolette-Malirat N, Maridonneau-Parini I. (2009) Three-dimensional migration of macrophages requires Hck for podosome organization and extracellular matrix proteolysis. *Blood.* Nov 6. [Epub ahead of print]
- Poincloux R, Al Saati T, Maridonneau-Parini I, Le Cabec V. (2009) The oncogenic activity of the Src family kinase Hck requires the cooperative action of the plasma membrane- and lysosome-associated isoforms. *Eur. J. Cancer* 45:321
- Vincent C, Maridonneau-Parini I, Le Clainche C, Gounon P, Labrousse A. (2007) Activation of p61Hck triggers WASp- and Arp2/3-dependent actin-comet tail biogenesis and accelerates lysosomes. *J Biol Chem.* 282, 19565-74
- Poincloux R, Cougoule C, Daubon T, Maridonneau-Parini I and Le Cabec V. (2007). Tyrosine-phosphorylated STAT5 accumulates on podosomes in Hck-transformed fibroblasts and chronic myeloid leukemia cells. *J. Cell. Physiol.*, 213(1), 212-20.
- Poincloux R, Vincent C, Labrousse A, Castandet J, Rigo M, Cougoule C, Bordier C, Le Cabec V and Maridonneau-Parini I. (2006). Physiopathological activation of Hck triggers re-arrangements of podosome structures in myeloid cells. *Eur. J. Cell. Biol.* 36(3), 779-788.
- Cougoule C, Carr  no S, Castandet J, Labrousse A, Astarie-Dequeker C, Poincloux R, Le Cabec V and Maridonneau-Parini I. (2005). Activation of the lysosome-associated p61Hck isoform triggers the biogenesis of podosomes. *Traffic*, 6(8):682-94.