



# Keehoon JUNG

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## Research Interests

Cancer Immunology, In Vivo Imaging, Single-Cell Genomics, Vascular Biology, Drug Development

## Education

- 2005 | B.S. in Biological Sciences, KAIST, Korea
- 2010 | Ph.D. in Biological Sciences and Biomedical Science & Engineering Program, KAIST, Korea

## Professional Career

- 2010-2013 | Research Fellow at Wellman Center (In Vivo Imaging), Harvard Medical School / MGH
- 2013-2018 | Research Fellow at Steele Laboratories for Tumor Biology, Harvard Medical School / MGH
- 2018- present | Assistant Professor, Seoul National University

## Honors

- 2018 | Milstein Award, International Cytokine & Interferon Society (ICIS)
- 2018-2027 | Creative- Pioneering Researchers Program, Seoul National University
- 2017 | Speaker Award, Gordon Research Conference - Angiogenesis
- 2016 | Bristol-Myers Squibb (BMS) Award, Tumor Immunology and Immunotherapy Meeting
- 2016 | AACR-GYRIG Scholar-in-Training Award, AACR Annual Meeting

## Publications

1. Choo YW, Jeong J, Jung K. Recent advances in intravital microscopy for investigation of dynamic cellular behavior in vivo. *BMB Reports*, (2020).
2. Jeong J, Suh Y, Jung K. Context drives diversification of monocytes and neutrophils in orchestrating the tumor microenvironment. *Frontiers in Immunology* (2019).
3. Jung K. et al., Targeting CXCR4-dependent immunosuppressive Ly6C(low) monocytes improves antiangiogenic therapy in colorectal cancer. *Proc Natl Acad Sci USA* (2017).
4. Jung K. et al., Ly6C(lo) monocytes drive immunosuppression and confer resistance to anti-VEGFR2 cancer therapy. *J Clin Invest* (2017).

# Real-time intravital characterization of non-classical monocytes in cancers

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Colorectal cancer (CRC) is the leading cause of cancer-related deaths worldwide. However, current anti-VEGF therapies for CRC provide limited survival benefit as tumors rapidly develop resistance to these agents.

We have developed a miniaturized confocal endomicroscopy technique for spontaneous CRC models in mice. We recently also established a novel abdominal imaging window. These unique systems enable us to monitor the CRC and its immune microenvironment longitudinally with a video-rate intravital multi-photon microscope. Using these in vivo imaging methods and CRC models, we have uncovered an immunosuppressive role for non-classical Ly6Clow monocytes that mediates resistance to anti-VEGFR2 treatment. We found that the chemokine CX3CL1 was upregulated in both human and murine tumors following the VEGF signaling blockade, resulting in recruitment of CX3CR1+ Ly6Clow monocytes into the tumor. We also found that treatment with VEGF-A reduced expression of CX3CL1 in endothelial cells. Intravital microscopy revealed that CX3CR1 is critical for Ly6Clow monocyte transmigration across the endothelium in tumors. Moreover, Ly6Clow monocytes recruit Ly6G+ neutrophils via CXCL5 and produce IL-10, which inhibits adaptive immunity. Preventing Ly6Clow monocyte or Ly6G+ neutrophil infiltration into tumors enhanced inhibition of tumor growth with anti-VEGFR2 therapy. Furthermore, we developed a gene therapy using a nanoparticle formulated with a siRNA against CX3CL1, which reduced Ly6Clow monocyte recruitment and improved outcome of anti-VEGFR2 therapy in mouse CRCs.

Taken together, we identified immunosuppressive non-classical Ly6Clow monocytes as key players in tumor resistance to anti-angiogenic therapy in CRCs. We also revealed molecular mechanisms underlying anti-angiogenic treatment resistance, suggesting potential immunomodulatory strategies to enhance the long-term clinical outcome of anti-VEGF therapies, proven by state-of-the-art in vivo imaging modalities.

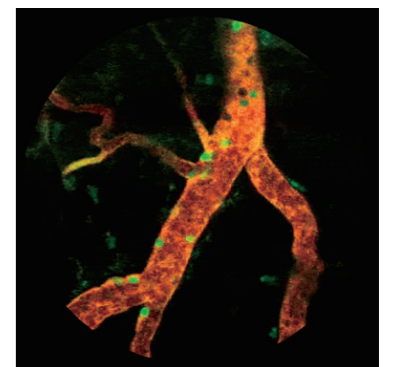


Fig. 1. Non-classical monocytes flow through blood vessels as they infiltrate tumors.

## References

- [ 1 ] Choo YW, Jeong J, Jung K. Recent advances in intravital microscopy for investigation of dynamic cellular behavior in vivo. *BMB Reports*, (2020).
- [ 2 ] Jeong J, Suh Y, Jung K. Context drives diversification of monocytes and neutrophils in orchestrating the tumor microenvironment. *Frontiers in Immunology* (2019).
- [ 3 ] Jung K. et al., Targeting CXCR4-dependent immunosuppressive Ly6C(low) monocytes improves antiangiogenic therapy in colorectal cancer. *Proc Natl Acad Sci USA* (2017).
- [ 4 ] Jung K. et al., Ly6C(lo) monocytes drive immunosuppression and confer resistance to anti-VEGFR2 cancer therapy. *J Clin Invest* (2017).
- [ 5 ] Jung K. et al., Endoscopic time-lapse imaging of immune cells in infarcted mouse hearts. *Circ Res* (2013).