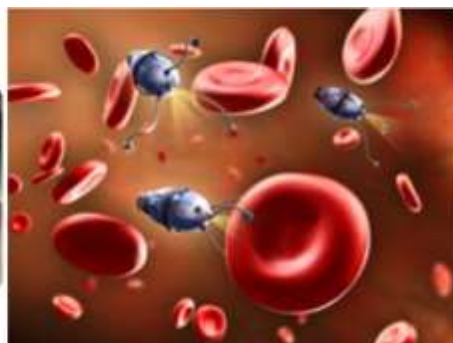


How to Assess Biological Activity of Inflammatory Plaque?: Combined OFDI-NIRF Molecular Imaging

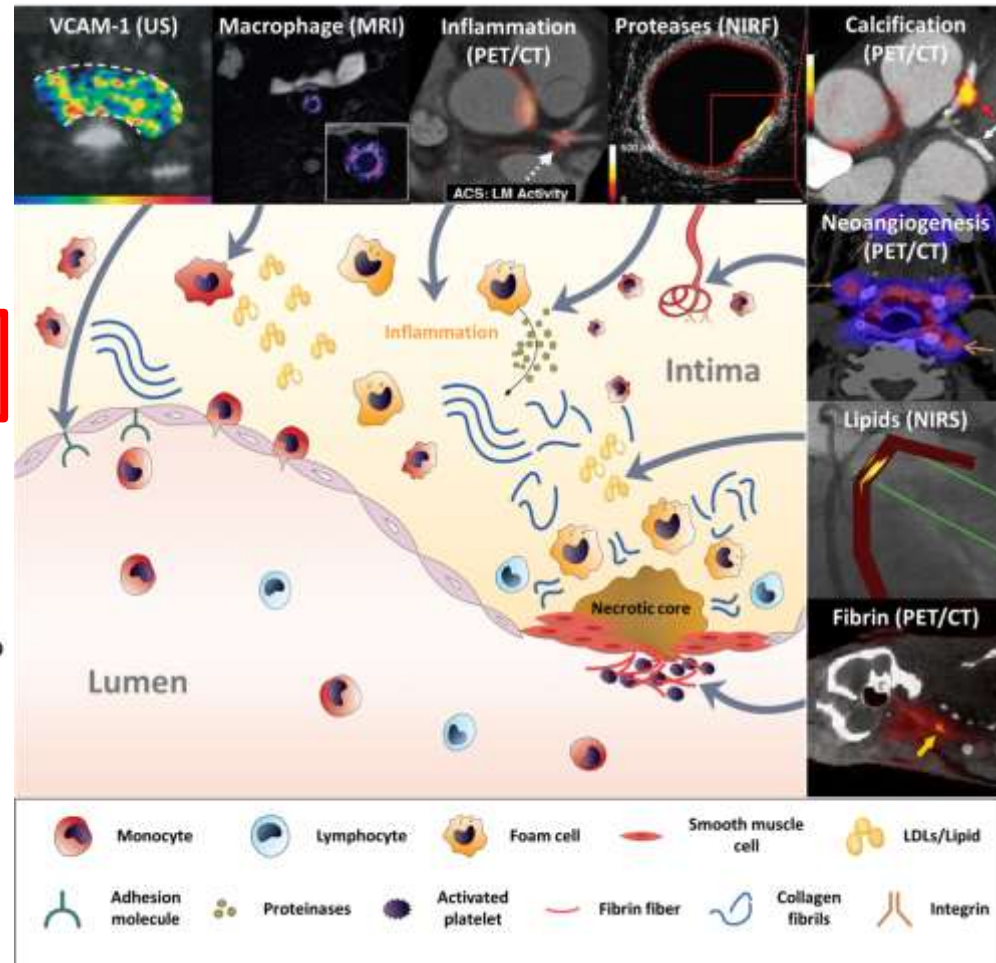
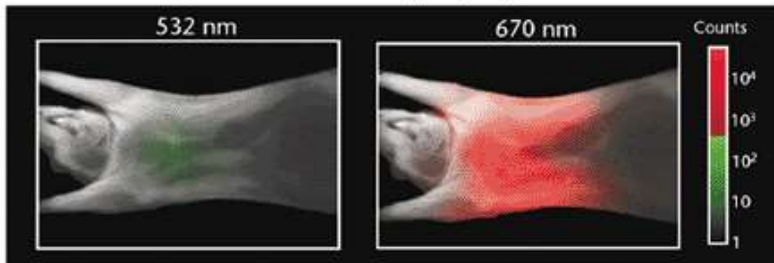
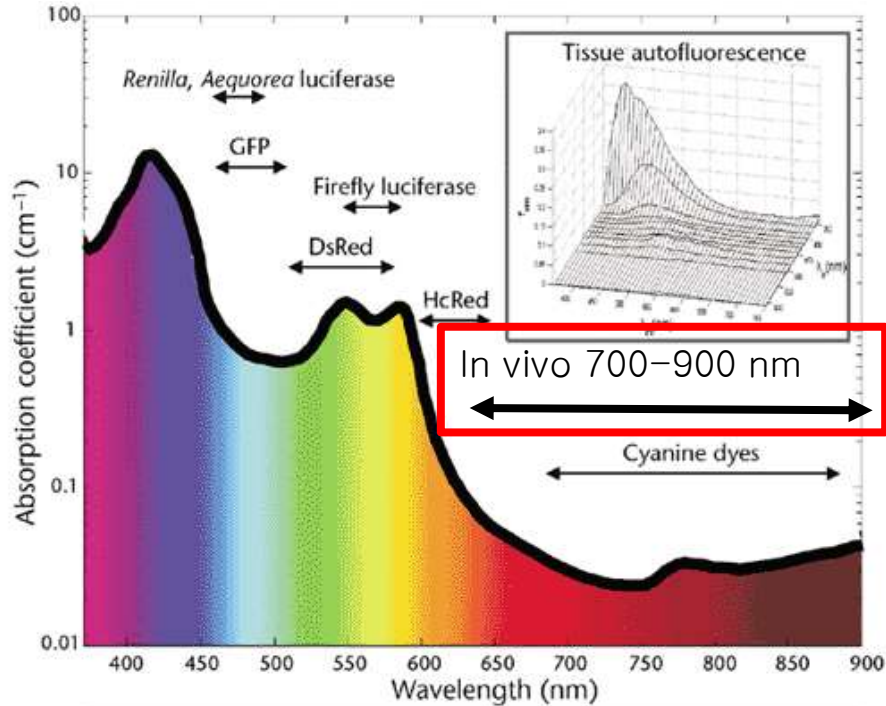
Kim Jin Won, M.D., Ph.D., F.A.C.C.



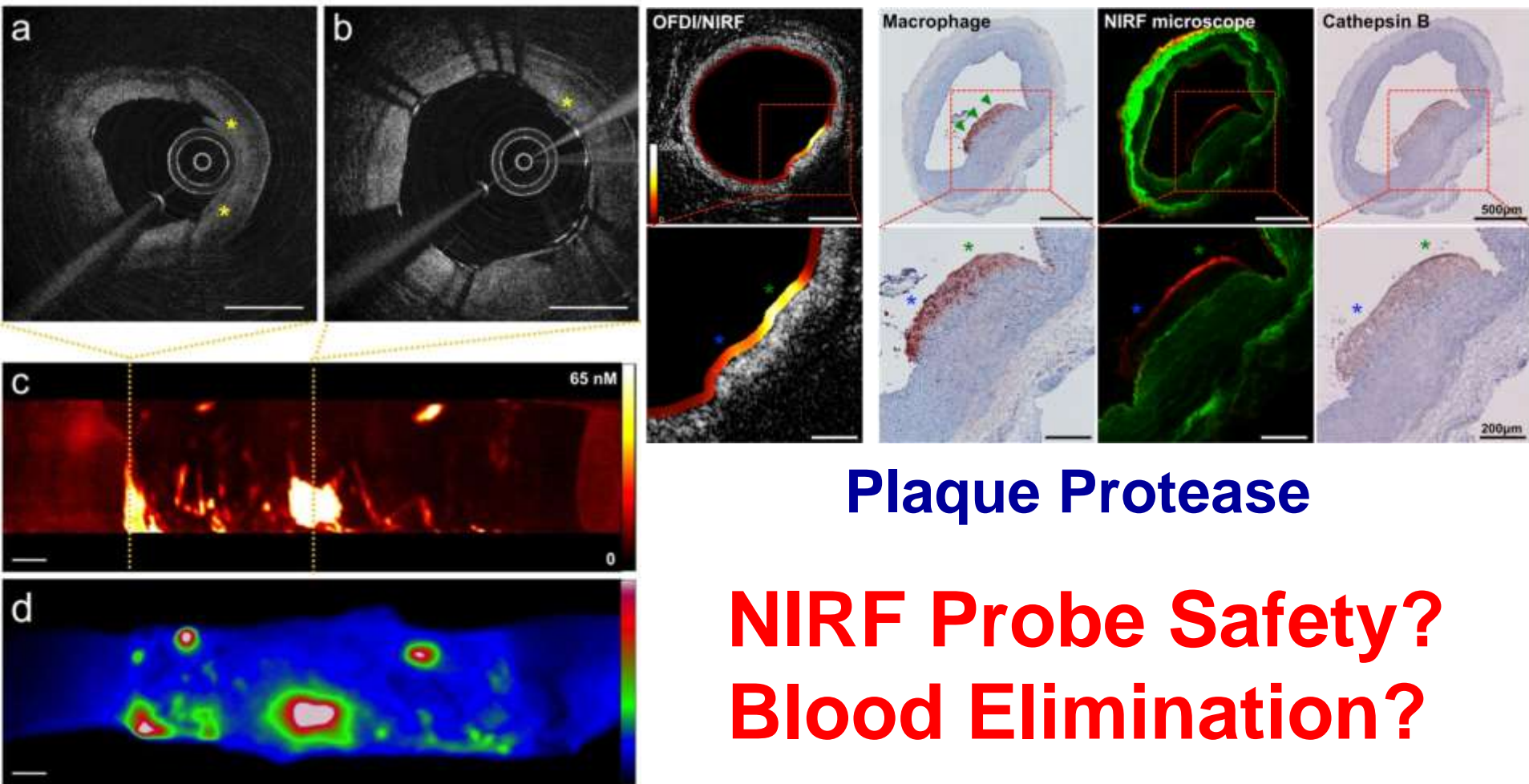
**Korea University Guro Hospital
Multimodal Imaging and Theranostic Lab**



MOLI with Near-infrared Fluorochrome (NIRF)



Fully Integrated OCT-NIRF Catheter



Plaque Protease

**NIRF Probe Safety?
Blood Elimination?**

**Fibrin-Targeting
Stent Thrombosis**

Kim JW et al. Nature Medicine 2011

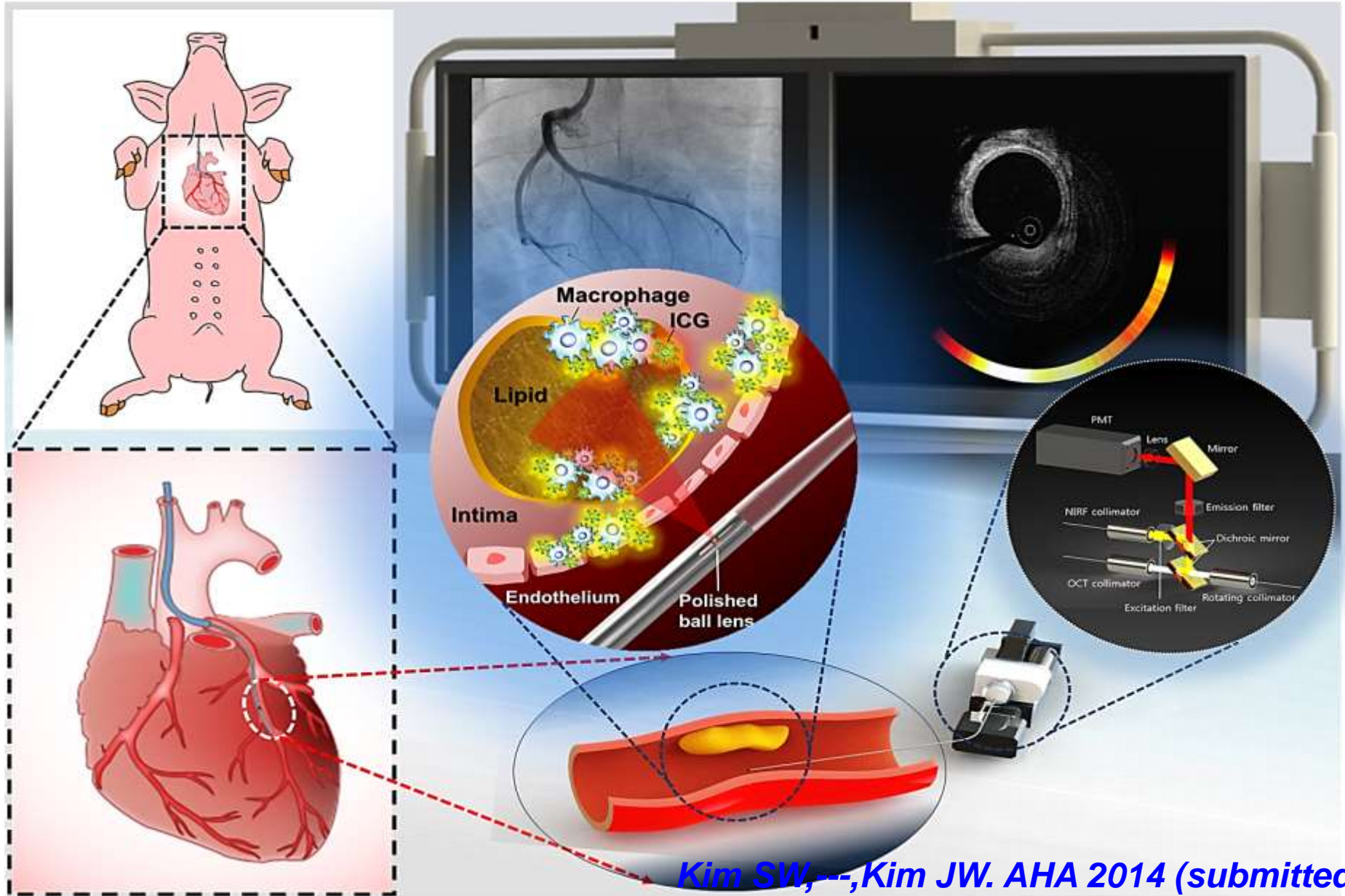
High-Speed 2nd Generation OCT-NIRF

Real-time data acquisition of OCT-NIRF

- Rotation speed: upto 100 rps
- Blood elimination: just flushing
- Pullback speed: upto 40mm/s
- No crosstalk
- **Real-time OCT-NIRF Synchronization**

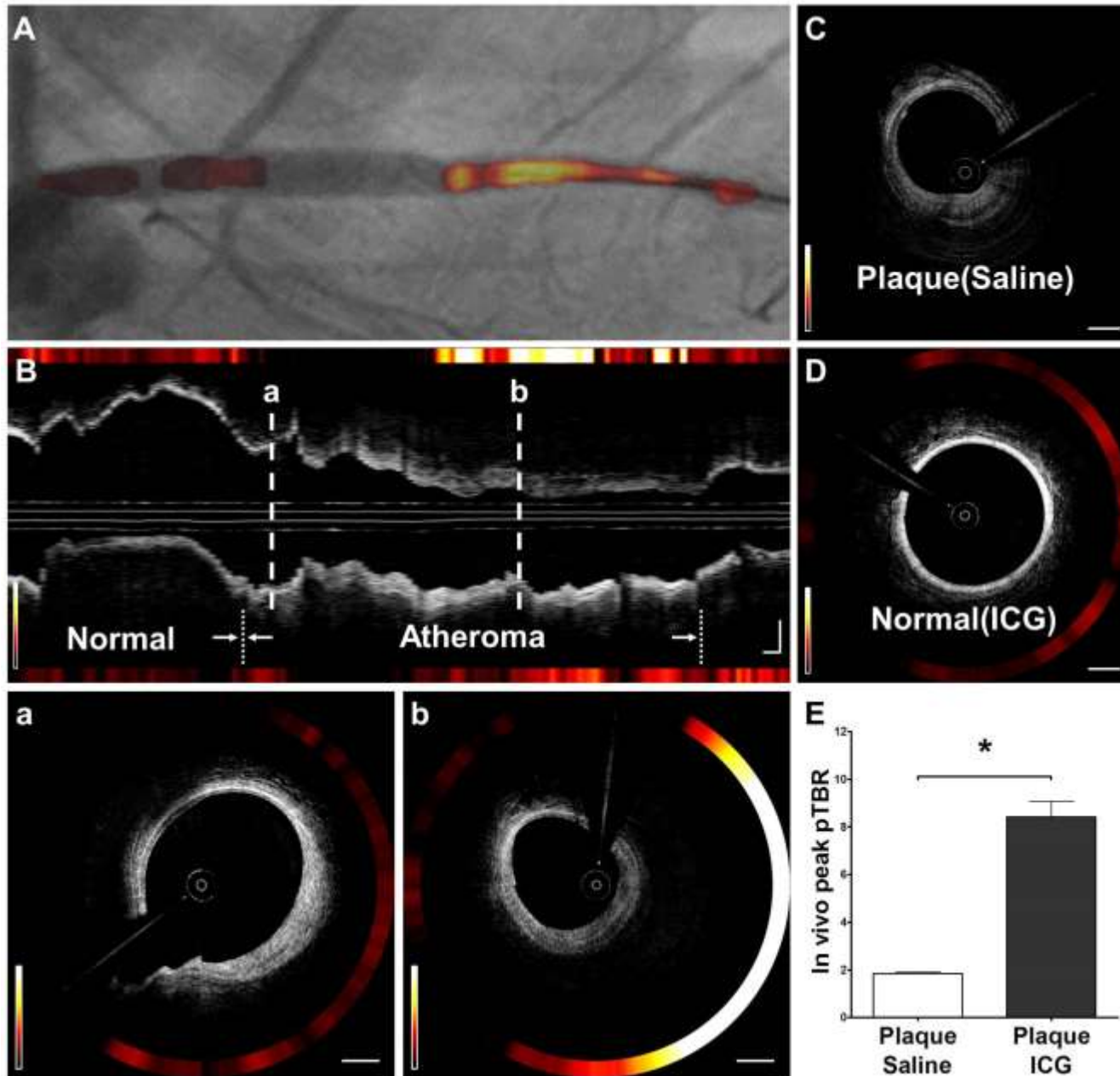


OCT-NIRF in a Beating Coronary Plaque

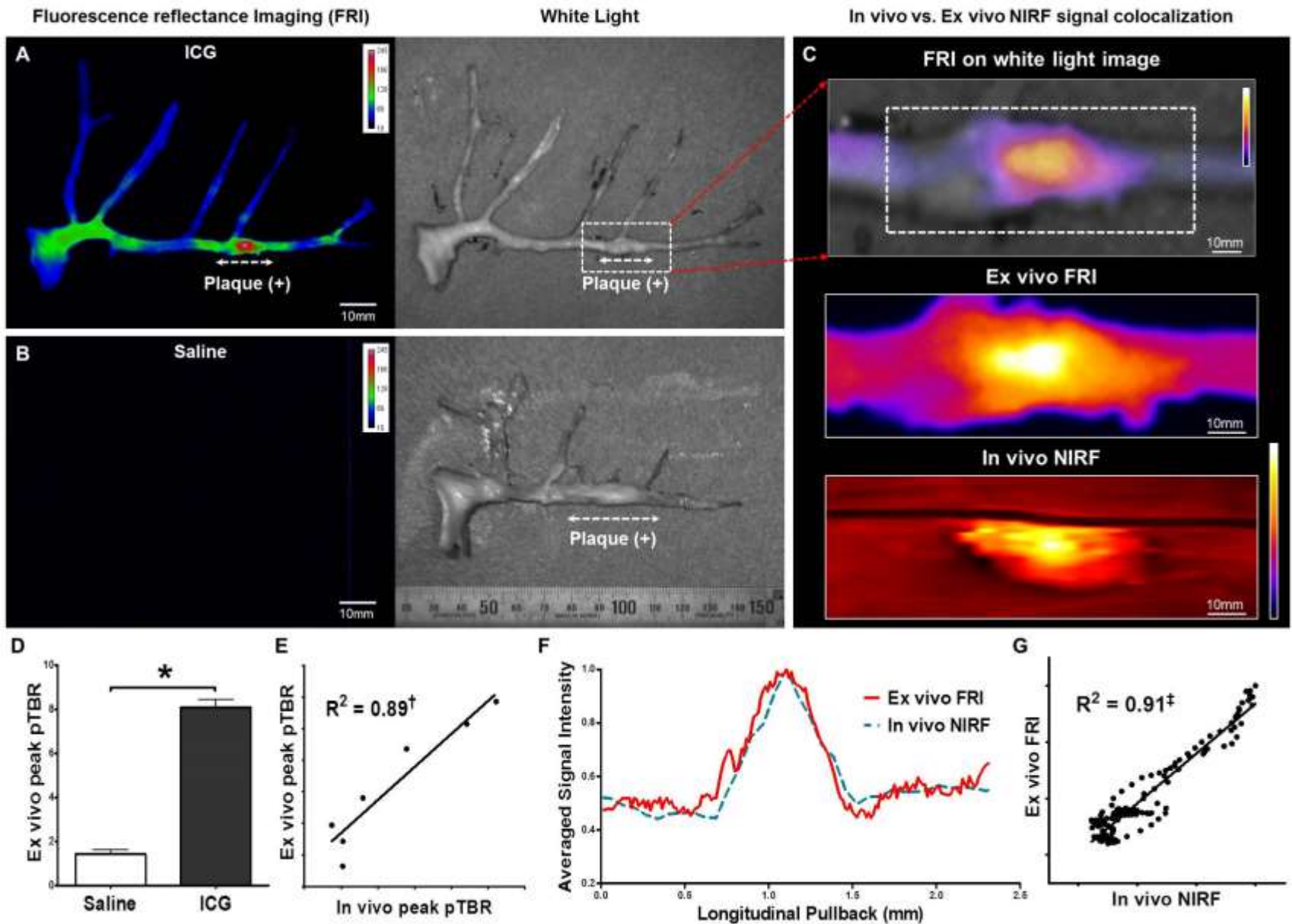


Kim SW, --, Kim JW. AHA 2014 (submitted)

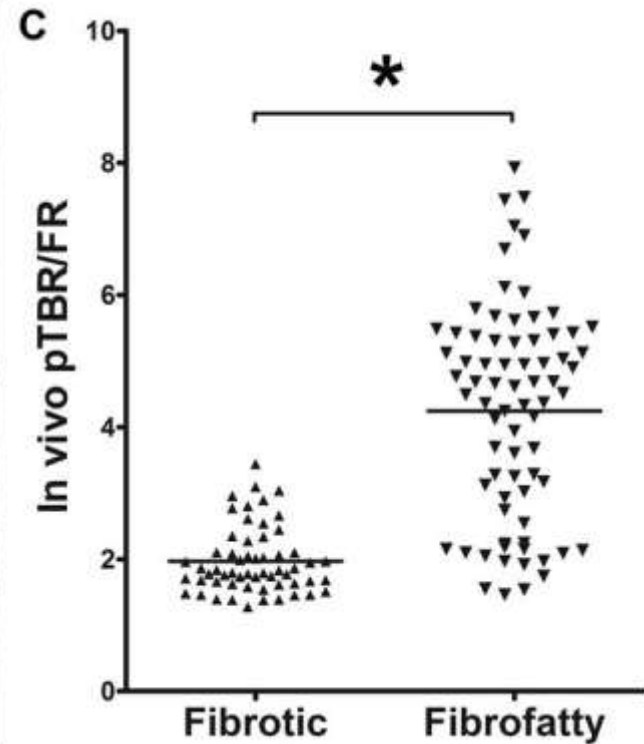
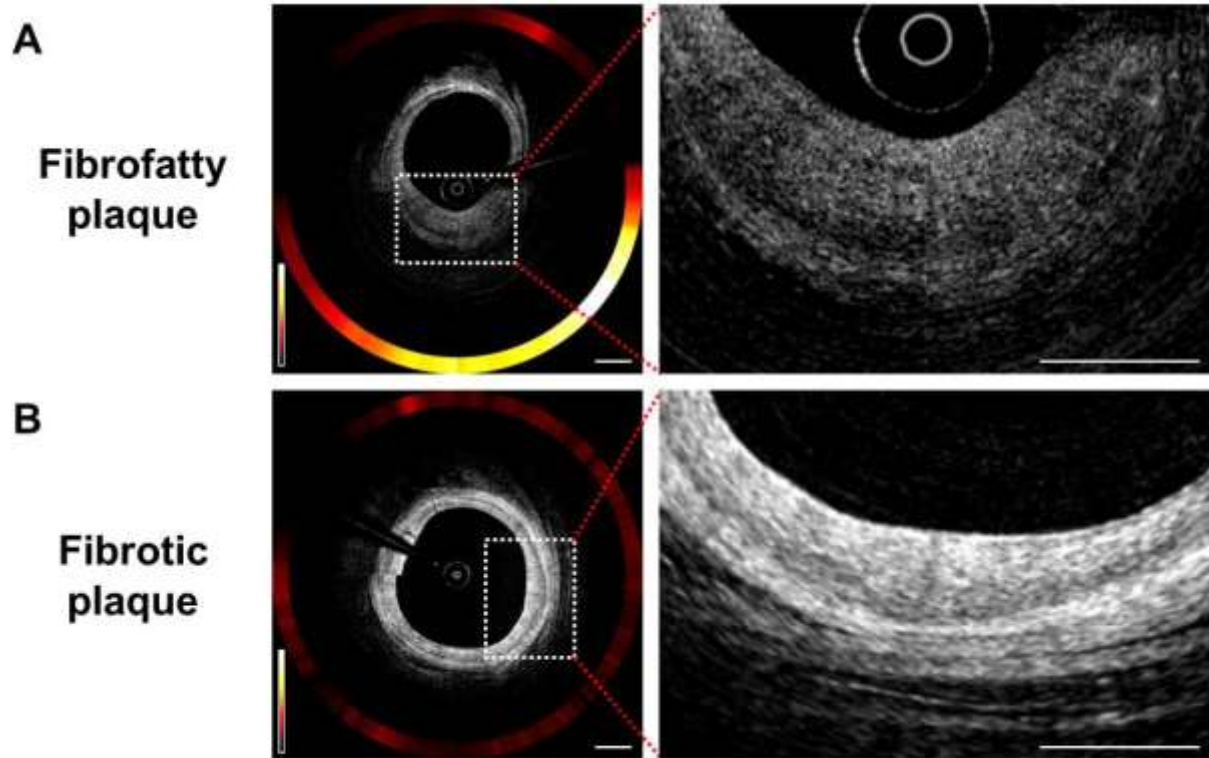
In Vivo OCT-NIRF



Ex Vivo Validation



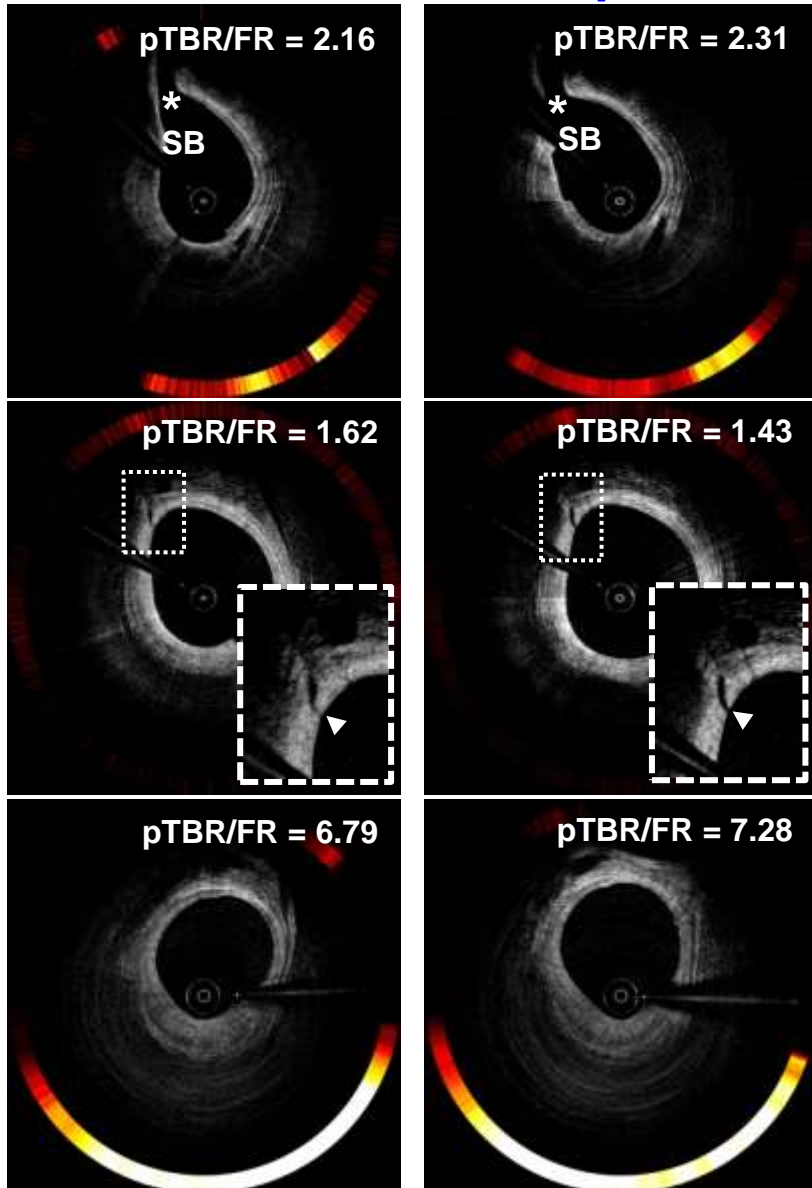
NIRF - Plaque Type



Excellent Reproducibility

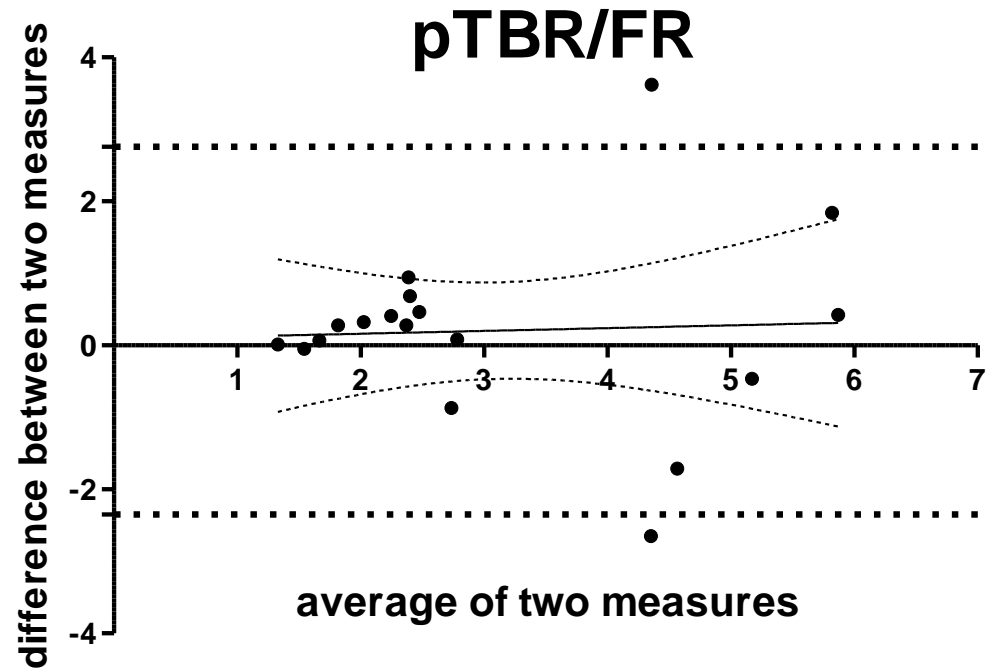
Initial

Repeat



ICC = 0.823 (82.3% consistency)

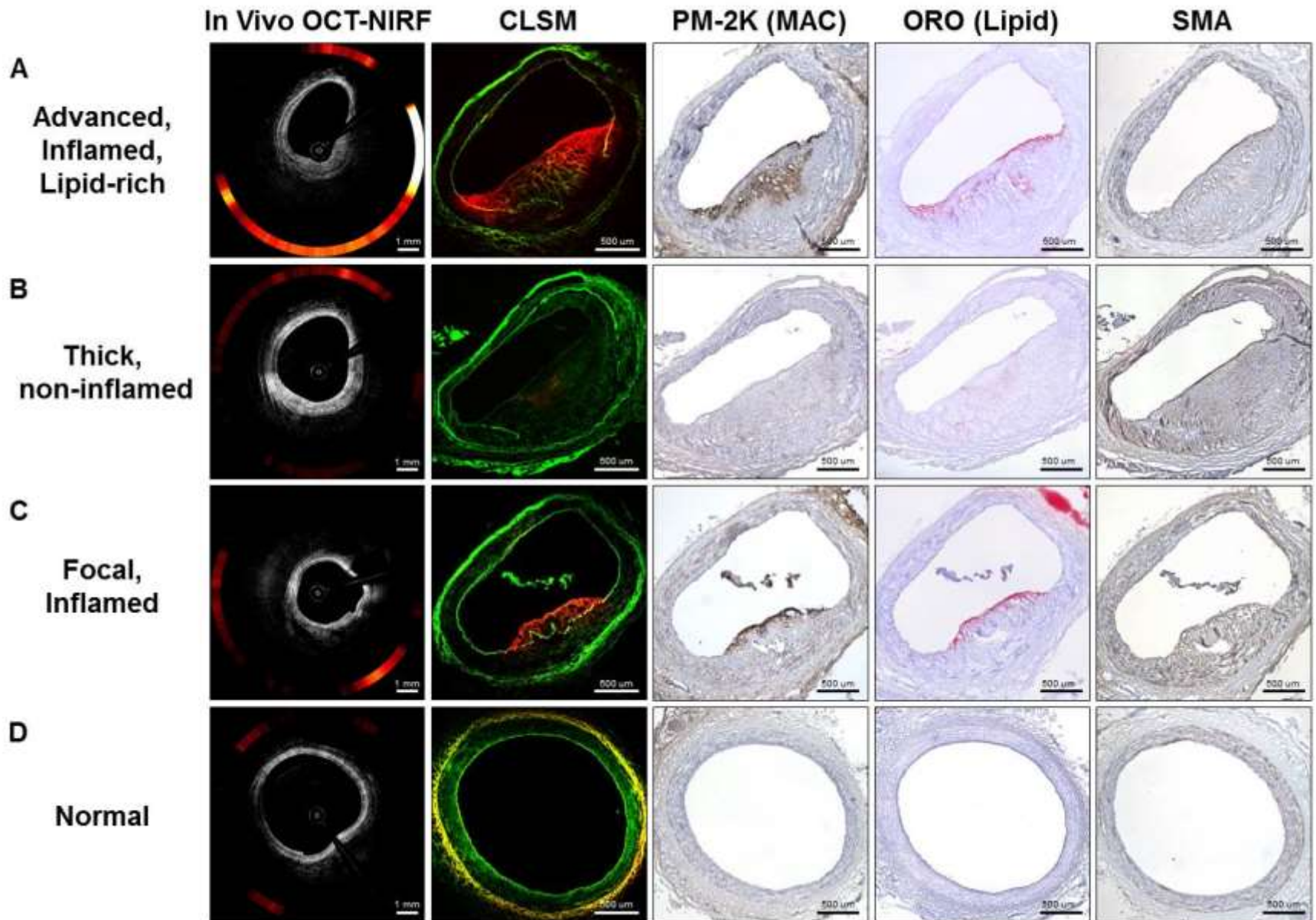
p < 0.001



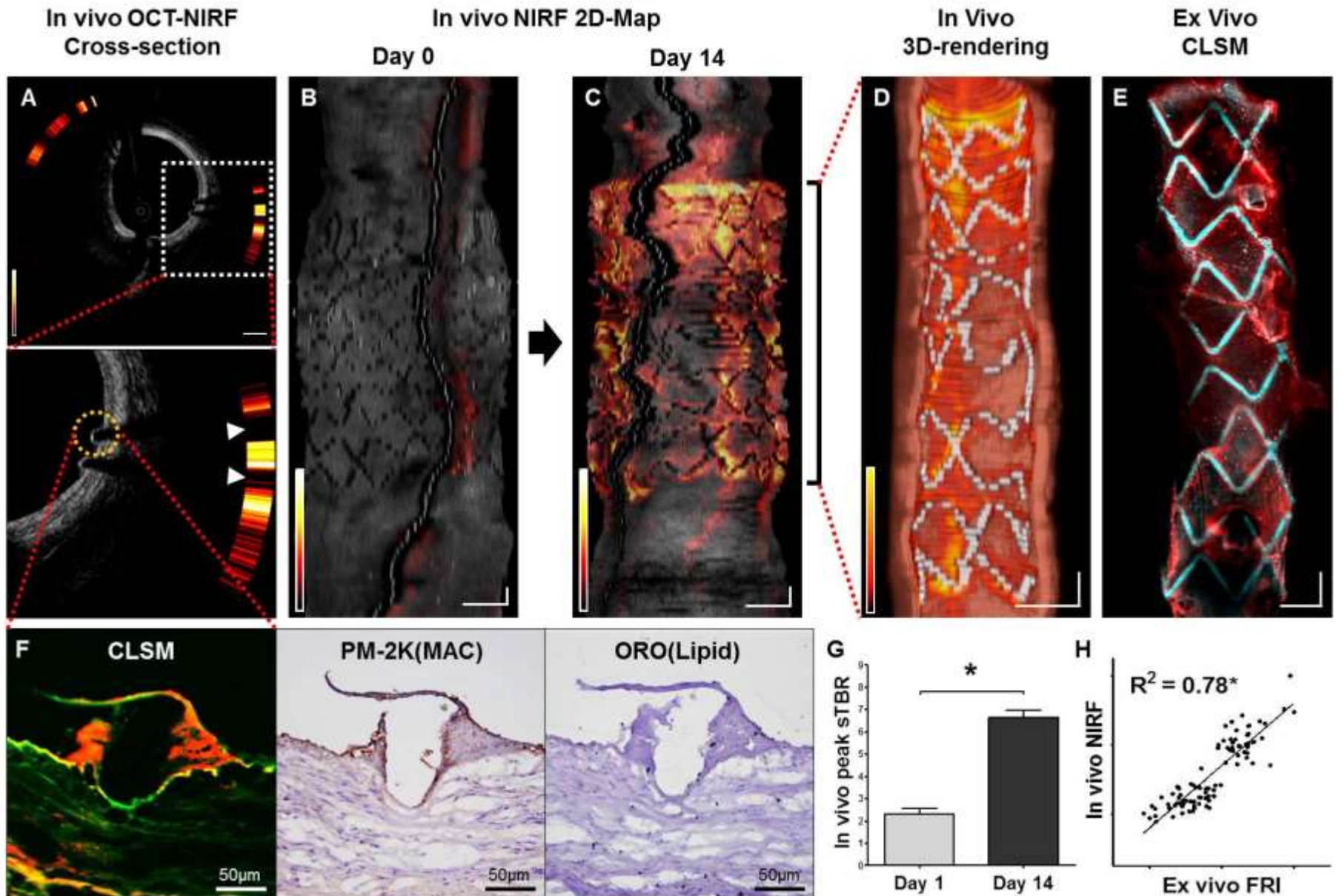
Bland-Altman Plot

ICC = Interclass Correlation Coefficient

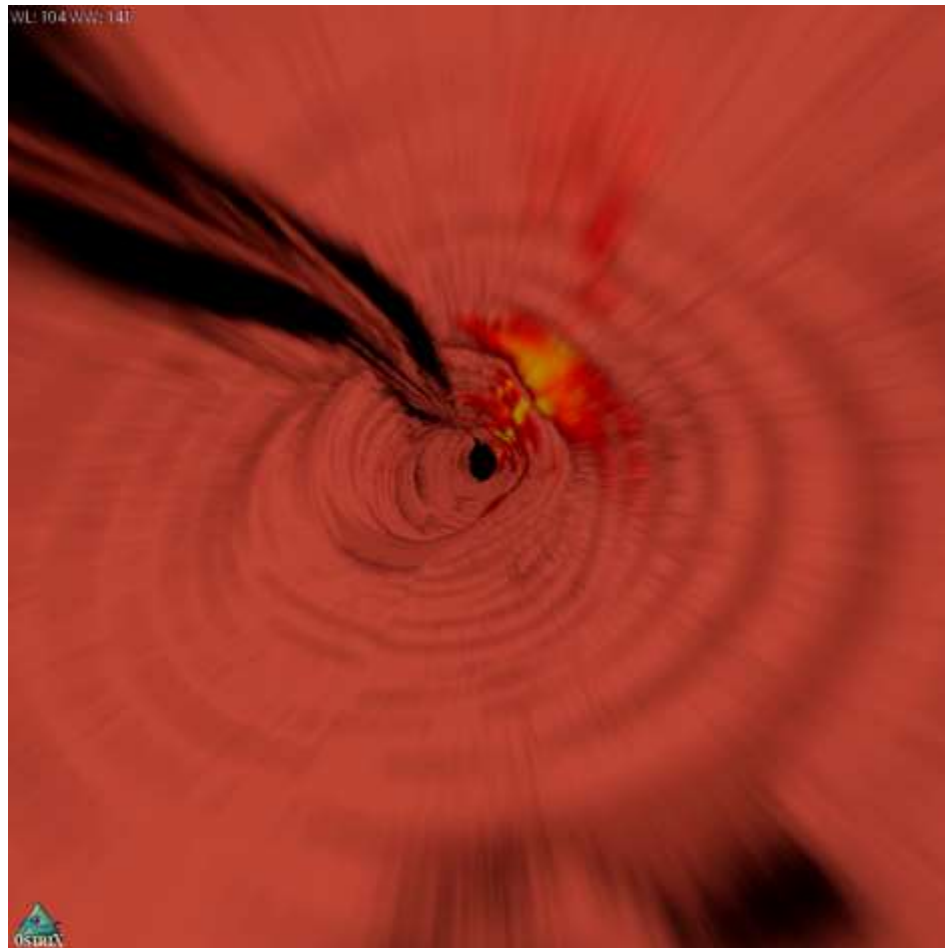
Corroborative Immunostaining



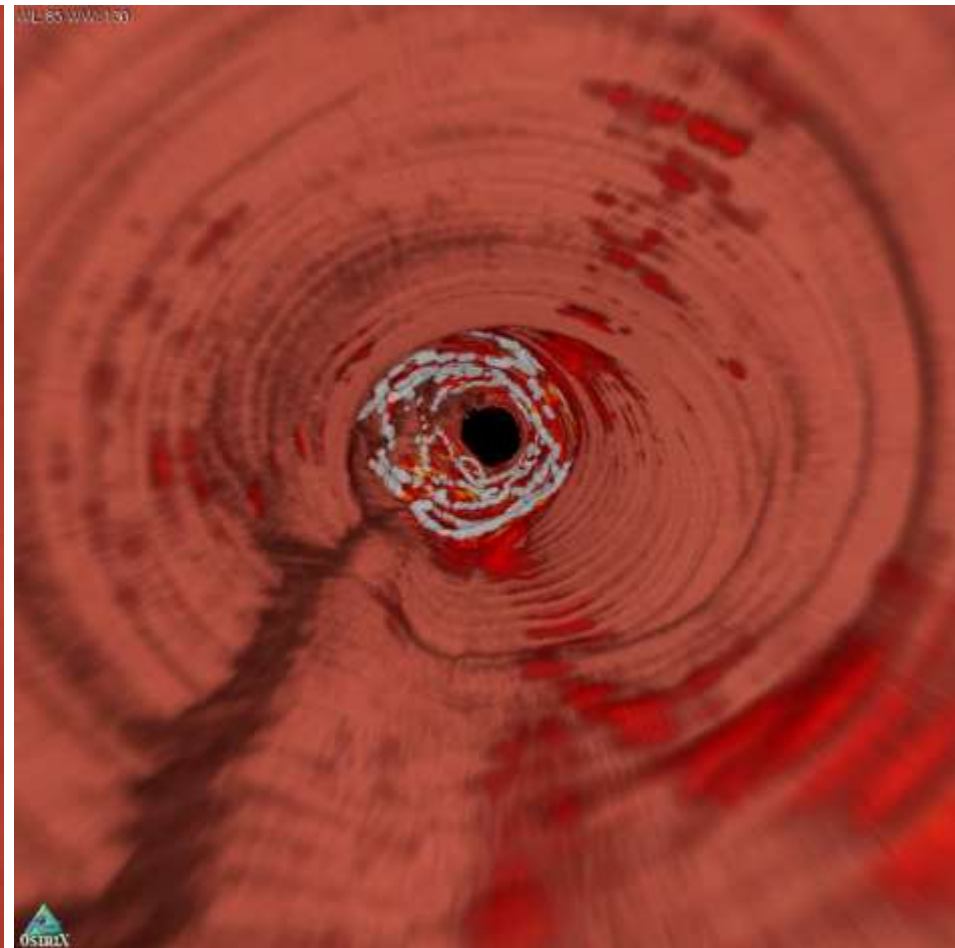
DES-associated Inflammation



Coronary OCT-NIRF Imaging *In Vivo*



Vulnerable Plaque

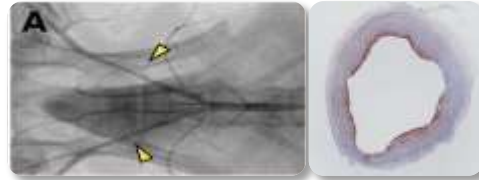


DES related inflammation

Clinical Trial Roadmap Launching

Preclinical

Fixed



Coronary,

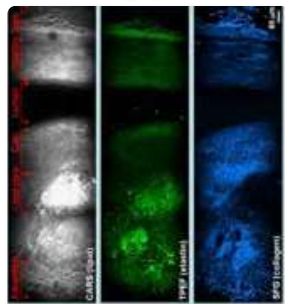


1st Human Trial

1 Autofluorescence

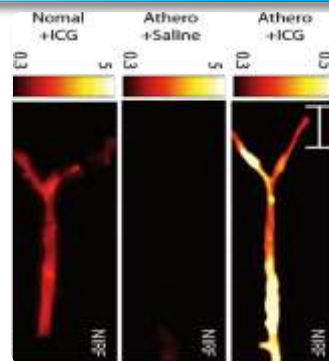
- Necrotic core signal
- Escape of nanoprobe

자가형광(lipid)



2 Macrophage Nonspecific

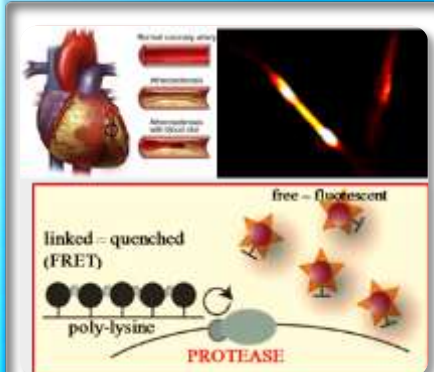
- ICG fluorochrome
- Validated human safety



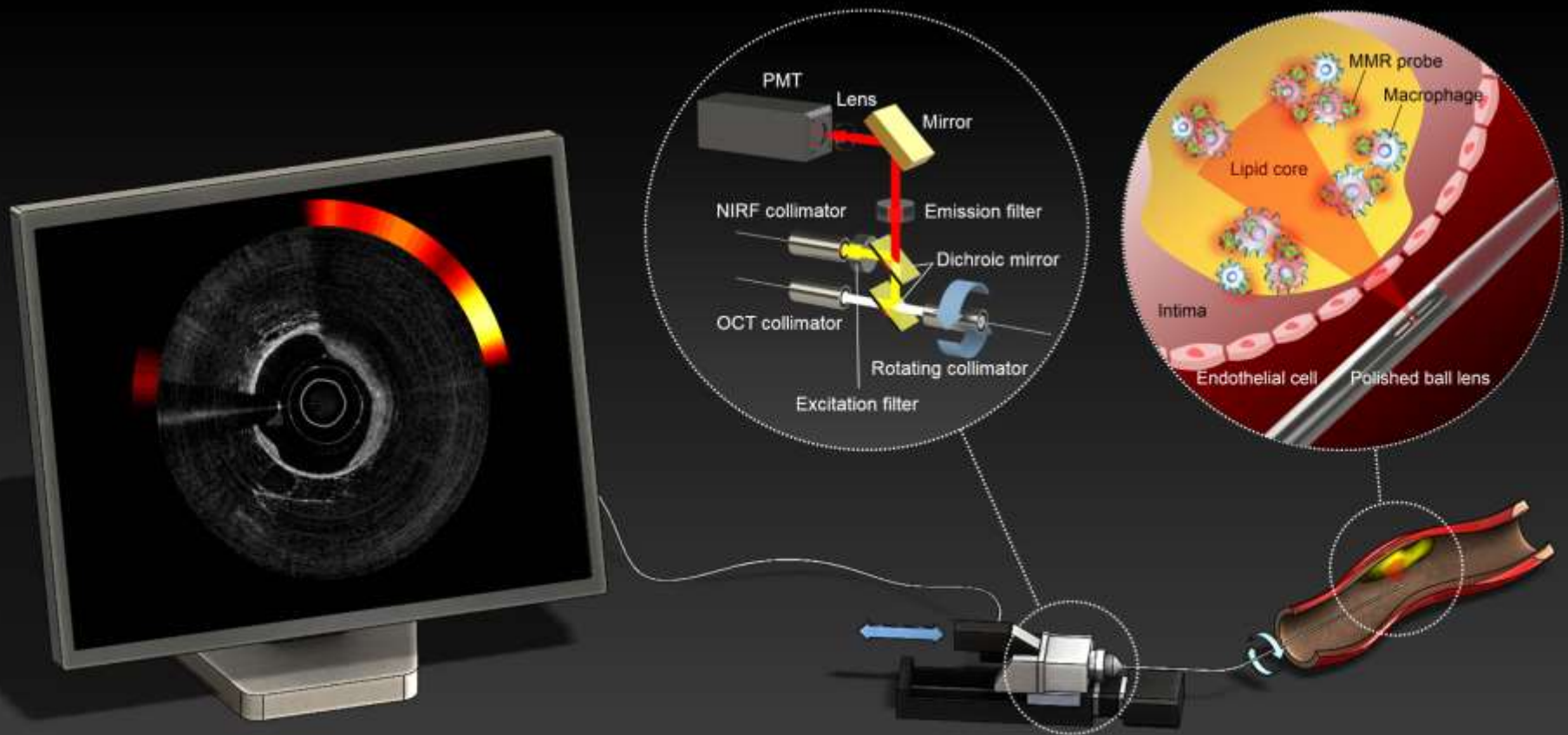
Science T. 2011

3 Specific targeting

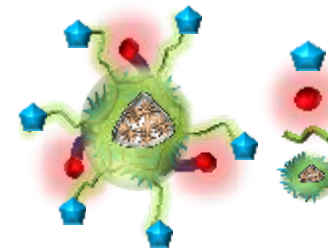
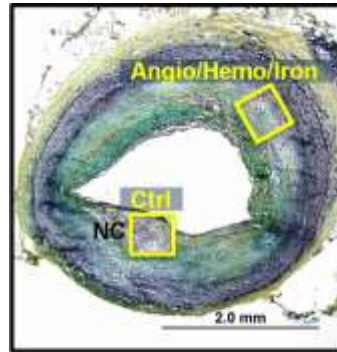
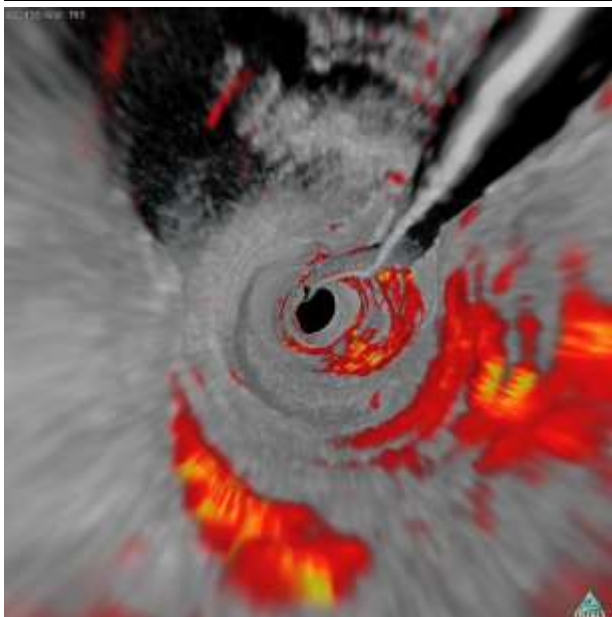
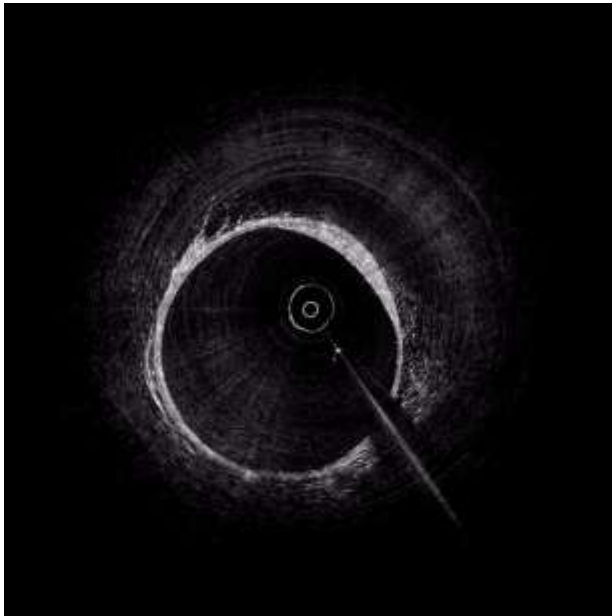
- Prosense VM 110
- Chitosan NIRF



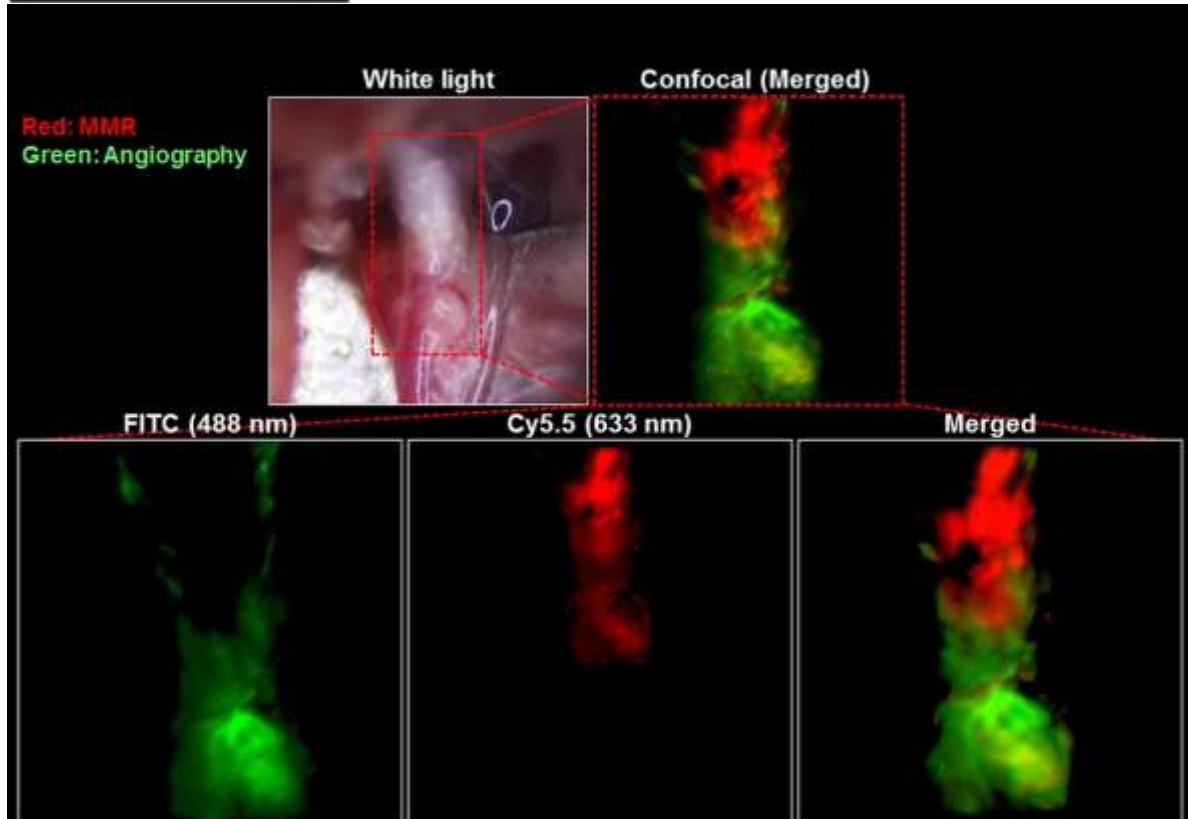
Targeting Strategy with a Novel Optical Probe



High-risk Plaque Mac Subset Imaging



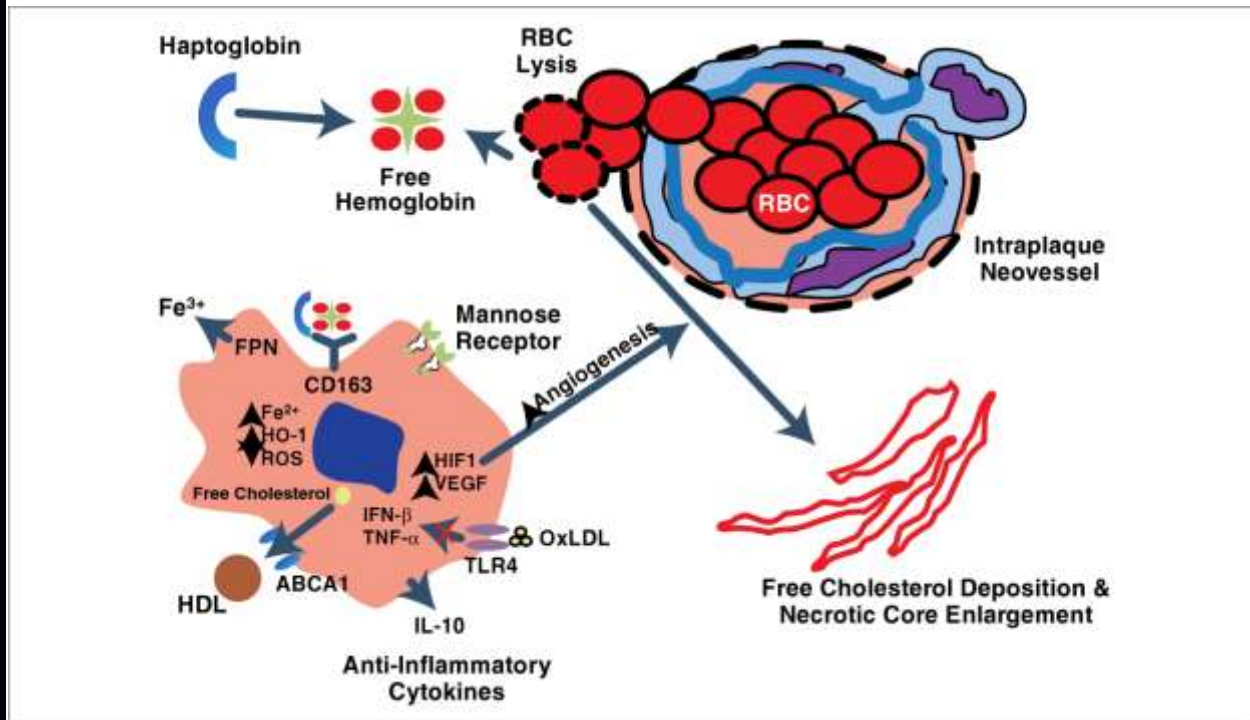
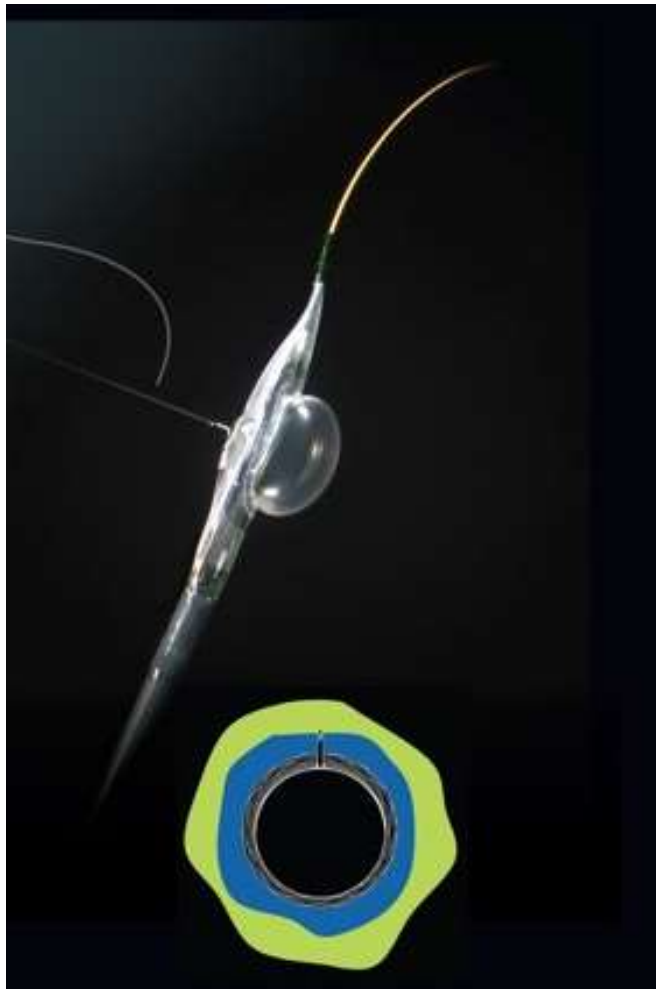
- Mannose receptor binding ligand
- NIRF dye (Cy5.5 or 7)
- PEG
- Glycol chitosan nanoparticle



submitted

In Vivo Plaque MMR MOLI

IPH May Modify Macrophage Subset Behavior?



OCT-Label Free FLIM Imaging

OCT-FLIM

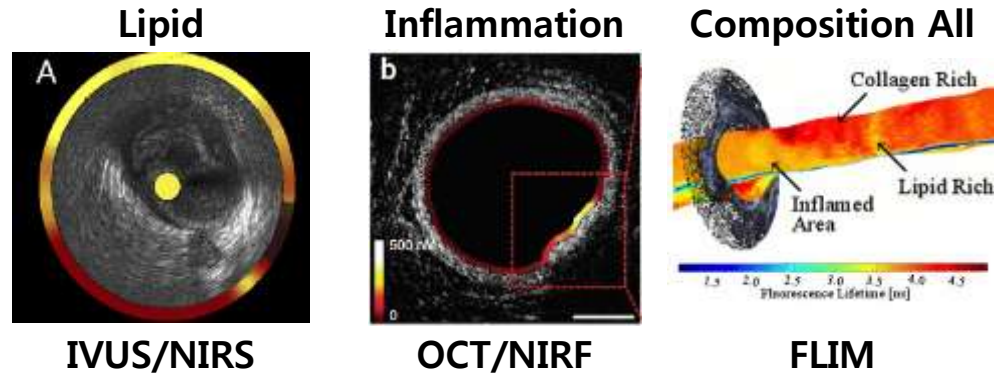
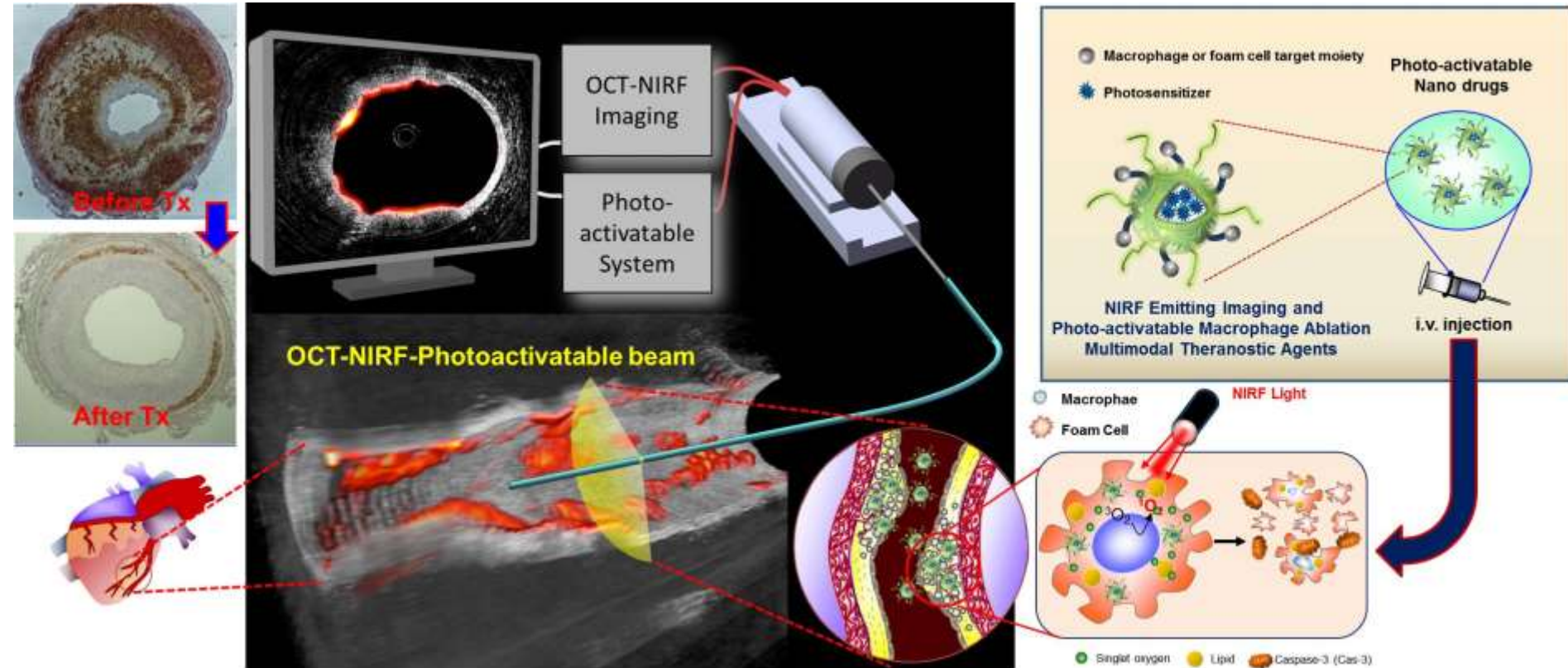


Table 1 Comparison between Intravascular Imaging Techniques

	X-ray angio.	IVUS	OCT	IVUS-NIRS	OCT-NIRF	OCT-FLIM
Resolution	+	++	+++	++	+++	+++
Speed	+++	+	+++	+	+++	+++
Lumen area	-	+++	+++	+++	+++	+++
TCFA	-	+	+++	++	+++	+++
Lipid plaques	-	+	+	+++	++	+++
Plaque burden	-	+++	+	+++	+	+
Thrombus	-	+	++	+	++	+++
Stent analysis	-	+	+++	+	+++	+++
Inflammation	-	-	+	-	+++	+++
Safety	+++	+++	+++	+++	+	+++

Personalized Theranostic Strategy



Conclusion

- A fully integrated OCT-NIRF imaging with a clinically approved NIRF enhancing ICG was able to accurately identify high-risk coronary plaque and assess DES-associated coronary inflammation.
- This highly translatable dual-modal, structural-molecular imaging strategy could enhance our capabilities to understand high-risk plaque biology and is expected to spur **personalized approaches** to estimate plaque vulnerability in near future.
- A newly developed, **plaque macrophage targeting NIRF probe** could be utilizable for high-risk plaque imaging, and needs to be further validated regarding acute toxicity and long-term safety.

Acknowledgements

Korea University, CV MT Lab

Jin Won Kim Byeong Won Cheon
Jae Joong Lee Sun Won Kim
Sunki Lee Ji Bak Kim
Ja Hyun Choi Eunjin Park
Joon Woo Song Hee Dong Kim
Woong Seo Sang Pyo Hong

Hanyang University, BME

Hongki Yoo Min Woo Lee
Jun Young Kim Chang-Soo Kim
Hyeong Soo Nam

Korea Basic Science Institute

Kyeongsoon Park Seung-Hae Kwon
Ok Kyu Park

KAIST, BPI Lab

Wang-Yuhl, Oh Han Sam Cho
Sun-Joo Jang Tae Shik Kim

KAIST, NOM Lab

DaeGab Gweon Jiheun Ryu

Funding

- National Research Foundation Funded by Korea Government to JW Kim, HK Yoo and KS Park (2012R1A2A2A046108)
- Basic Science Research Program through NRF by MEST to HK Yoo (2012R1A1A1041203),
- Korean Vascular Research Working Group R&D grant to JW Kim (2012R1200691),
- KUMC Special R&D grant to JW Kim (2012K1220481)