Identification of Cav1 Domains Using Super Resolution Microscopy and Machine Learning

Ismail M. Khater \textsuperscript{1}, Ivan R. Nabi \textsuperscript{2}, Ghassan Hamarneh \textsuperscript{1}

\textsuperscript{1} Medical Image Analysis Lab, School of Computing Science, Simon Fraser University, Burnaby, BC V5A 1S6, Canada, Burnaby, Canada
\textsuperscript{2} Department of Cellular and Physiological Sciences, Life Sciences Institute, University of British Columbia, Vancouver, BC V6T 1Z3, Canada, Vancouver, Canada

We have developed graph and machine learning-based methods to analyze Single Molecule Localization Microscopy (SMLM) super-resolution of caveolin-1 (Cav1) data. We represent SMLM localizations as a graph, where Cav1 molecules are modeled as nodes with edges connecting nodes to encode molecular interaction. We reduce the effect of multiple blinking via iterative merging. We denoise the data by comparing the per-node features with random network features\cite{1}. Then, we segment the filtered molecules into isolated blobs\cite{1} for further per-blob analysis. Finally, we identify the biological class of each blob based on machine and deep-learning approaches using hand-designed\cite{1}, graphlet-based\cite{2}, and deep-learning features\cite{3}.

By matching Cav1 classes from PC3 and CAVIN1 transfected PC3 cells, our results show four classes of Cav1 domains (caveolae, S2 hemispherical scaffolds, and small scaffolds S1A and S1B)\cite{1-3}. Network modularity analysis of endogenous Cav1 in HeLa cells suggests that S1B scaffolds are dimers of S1A scaffolds and that larger S2 scaffolds and caveolae are modular structures formed from multiple units of smaller S1A and S1B scaffolds respectively\cite{4}.

1. Khater et al., 2018, Scientific-Reports
2. Khater et al., 2019, Bioinformatics
3. Khater et al., 2019, bioRxiv,526327
4. Khater et al., 2018, bioRxiv,495382

Supported by CIHR PJT-159845,PJT-156424 and NSERC Discovery grants (IRN,GH).