Abstract Submitted
for the MAR16 Meeting of
The American Physical Society

Autophagy selectivity through receptor clustering ANDREW RUTENBERG, AIDAN BROWN[1], Dalhousie University — Substrate selectivity in autophagy requires an all-or-none cellular response. We focus on peroxisomes, for which autophagy receptor proteins NBR1 and p62 are well characterized. Using computational models, we explore the hypothesis that physical clustering of autophagy receptor proteins on the peroxisome surface provides an appropriate all-or-none response. We find that larger peroxisomes nucleate NBR1 clusters first, and lose them due to competitive coarsening last, resulting in significant size-selectivity. We then consider a secondary hypothesis that p62 inhibits NBR1 cluster formation. We find that p62 inhibition enhances size-selectivity enough that, even if there is no change of the pexophagy rate, the volume of remaining peroxisomes can significantly decrease. We find that enhanced ubiquitin levels suppress size-selectivity, and that this effect is more pronounced for individual peroxisomes. Sufficient ubiquitin allows receptor clusters to form on even the smallest peroxisomes. We conclude that NBR1 cluster formation provides a viable physical mechanism for all-or-none substrate selectivity in pexophagy. We predict that cluster formation is associated with significant size-selectivity.

[1]now at Simon Fraser University

Andrew Rutenberg
Dalhousie University

Date submitted: 06 Nov 2015 Electronic form version 1.4