Biochemistry Cumulative Examination
Chemical Biology
4 April 2019

Total: **100 points**

(**1**) What is the major function of the lysosome in cells? (10 points)

(**2**) What is the pH inside the lysosome? Is it acidic, basic, or neutral? How is this pH gradient maintained? (10 points)

(**3**) What are three ways that lysosome function can be inhibited? (15 points)

(**4**) What does the accumulation of LC3-II tell you? What is another method that can be used to measure LC3-II accumulation besides the GFP-LC3 microscopy-based assay? (10 points)

(**5**) What observation(s) supports the conclusion that BRD1240 does not nonspecifically accumulate in lysosomes to exert its function? (10 points)

(**6**) How does the assay for autophagosome formation and maturation (flux) enable the distinction between autophagy activators and late-stage inhibitors? What are the mechanisms of PI-103 and bafilomycin A1? Why were they used in this experiment? (15 points)

(**7**) What major conclusions were made from the structure-activity relationship studies? (10 points)

(**8**) What key experiment was used to determine that BRD1240 has a similar activity to bafilomycin A1? How does this experiment provide this information? (10 points)

(**9**) In the membrane fraction assay to determine the effect of BRD1240 on V-ATPase activity, what was required to observe lysosomal deacidification? How do the results compare to bafilomycin A1? What conclusions does this allow you to make about the mechanism of BRD1240? (10 points)