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Universiteit Leiden



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**Title:** Applications for activity-based probes in biomedical research on glycosidases

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# Propositions (Stellingen)

## *Accompanying the thesis*

Applications for activity-based probes in biomedical research on glycosidases

Chi-Lin Kuo

1. Mechanism-based suicide inhibitors for glycosidases can be chemically appended with a reporter group that allows unprecedented sensitive and specific visualization of the reacted (and labeled) active enzyme molecules.  
*This thesis, Chapter 1*
2. Conduritol B epoxide (CBE) can be used to generate authentic cell and animal models of Gaucher disease, whilst cyclophellitol—a closer  $\beta$ -glucose mimetic and a much more potent inhibitor of glucocerebrosidase, cannot.  
*This thesis, Chapter 2*
3. Replacing the BODIPY moiety with a bulky hydrophobic group enables the C8-substituted cyclophellitol to effectively inactivate glucocerebrosidase in the brain of tested animals.  
*This thesis, Chapter 3*
4. The configuration of cyclophellitol aziridines accurately predicts their selectivity for target glycosidases, but not their potency.  
*This thesis, Chapter 4–7*
5. The broad reactivity of a given activity-based probe can be both disadvantageous and advantageous, depending on the type of application.  
*This thesis, General Discussion*
6. Despite the development of novel activity-based probes, improved methods for detecting active glycosidases molecules *in vivo* are still warranted.  
*This thesis, General Discussion*
7. Activity-based protein profiling, immunoblotting, and (fluorogenic) enzymatic assay, when combined, may give the most comprehensive biochemical analysis in the research of lysosomal storage diseases.  
*This thesis, General Discussion*
8. The alkyl linker part of a cyclophellitol aziridine activity-based probe could be the overlooked element in dictating the probe's target selectivity.  
*This thesis, General Discussion*
9. Getting a PhD: “A ride from the pinnacle of student world to the bottom of professional world.”  
*Joshua Schimel, “Writing Science”*
10. Anything is possible, including surviving the Dutch botterham lunch.
11. “A conversation with a wise person is worth of ten years' study of books.”  
*Chinese proverb*