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Leiden
The Netherlands

Breathing in thin air: structure, function and therapeutic opportunities of bd type oxidases

Velden, T.T. van der

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Propositions

Accompanying the thesis

Breathing in Thin Air:

Structure, Function, and Therapeutic Opportunities of *bd* type Oxidases

1. Enzyme activity of *M. tuberculosis* cytochrome *bd* is redox regulated by the Q-loop disulfide bond, which allows for the rapid activation seen *in vivo*.

Chapter 2

2. A quinone binding site in a quinol oxidase does not automatically constitute a turnover site.

Chapter 2&3

3. The traditional emphasis on static protein structures limits our understanding of how controlled disorder enhances catalytic efficiency.

Chapter 3&6

4. Structural prediction enables conceptual leaps in hypothesis generation.

Chapter 5

5. Heterogeneity in respiratory enzyme redundancy among pathogens limits the potential for a broad-spectrum respiratory chain inhibitor.

6. To battle antibiotic resistance is to battle evolution. Without a shift in strategy, evolution will win.

7. The terminology "terminal oxidase" is an oversimplification of the integrated role of cytochrome *bd* in the defense against bacterial stressors.

8. *In vitro* binding affinity to human respiratory chain proteins is not a sufficient predictor of cytotoxicity.

9. Scientific progress depends on continuously challenging one's own narrowed perspectives.

10. In research, creativity and experience are equally important.

11. Solutions to specific problems are frequently obscured by disciplinary boundaries rather than absence of knowledge.

12. The struggle of climbing the mountain is what makes the view most special.

Tijn T. van der Velden
Leiden, 2 september 2026