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Universiteit Leiden



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Title: Autotaxin : biochemical and functional studies

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PROPOSITIONS

Belonging to the thesis

Autotaxin, biochemical and functional studies

- 1- The enzyme autotaxin (ATX) is expressed in breast cancer, but ATX expression levels are not a prognostic factor for clinical outcome (*this thesis*)
- 2- Activity-dependent probes are useful tools to monitor ATX activity in biological fluids (*this thesis*)
- 3- The long isoform of ATX (ATX α) contains a unique insertion in the catalytic domain. Cleavage of this insert by furin does not result in loss of activity, but could serve to regulate the interaction between ATX α and heparan sulfate proteoglycans (*this thesis*)
- 4- Binding of ATX α to heparin suggests a new mechanism for localized LPA production and signaling by binding of ATX α to heparan sulfate proteoglycans at the cell membrane (*this thesis*)
- 5- Deletion of an 18-amino acid stretch in the catalytic domain of ATX compared to its nucleotide pyrophosphatase/phosphodiesterase (NPP) family members allows the formation of a lysophospholipid binding pocket. The presence of this stretch explains why the NPP1 and NPP3 family members of ATX cannot function as a lysophospholipase (*Hausmann et al, Nat Struct Mol Biol 2011; 18(2): 198-204* and *Nishimasu et al, Nat Struct Mol Biol 2011; 18(2): 205-12*)
- 6- The rigid interaction between the inactive nuclease domain and the active catalytic domain in the ATX structure is a clever evolutionary solution to maintain stability of the catalytic domain (*Moolenaar & Perrakis, Nat Rev Mol Cell Biol 2011; 12(10): 674-79*)
- 7- Studies to understand the behavior of tumor cells should not solely focus on the traits of tumor cells, but instead must include the contributions of the tumor environment as well (*Hanahan & Weinberg, Cell 2011; 144(5): 646-74*)
- 8- Absence of evidence is not evidence of absence (*Altman & Bland, B M J 1995; 311(7003): 485*)
- 9- Contrary to the expectation that science will reveal one single clear answer, more often than not scientists have to be satisfied with several answers and even more questions as a result
- 10- The human genome is like a book of 23 chapters (the “chromosomes”) with in total over three billion letters (the “nucleotides”). The fact that we comprehend only around 2% of this text indicates that we have not finished reading yet
- 11- If you do not learn from your mistakes, you make a mistake (*Johan Cruijff*)
- 12- The world is a book, and those who do not travel read only one page (*Aurelius Augustine, Roman philosopher, 354-430*)