MT1-MMP Pathway Analysis Using Mathematical Model

Takashi Suzuki

Division of Mathematical Science, Graduate School of Engineering Science, Osaka University,
Machikaneyamacho, Toyonaka 560-8531, Japan

MT1-MMP is a potent invasion-promoting membrane protease employed by aggressive cancer cells. MT1-MMP localizes preferentially at membrane protrusions called invadopodia where it playsa central role in degradation of the surrounding extracellular matrix (ECM). While MT1-MMP degrades collagen I, II, III and laminin 1, 5, it also activates a secretive basal membrane enzyme MMP2. Thus MT1-MMP activates MMP2 which degrades basal membrane made by collagen IV. After this basal membrane is degraded, MT1-MMP itself degrades ECM also. Here the other molecule TIMP2 is involved by this process. We construct a mathematical model for this process, examine its validity, and executed numerical simulations of modified models reflecting biological settings. The contribution of rapid turnover ispredicted in this way, which has been confirmed by FRAP analysis. Having described the process of this discovery, we show a remarkable mathematical structure of this model, in the context of the theory of dynamical systems.

Takashi Suzuki
Professor, Division of Mathematical Science
Graduate School of Engineering Science, Osaka University, Japan
E-mail: suzuki@sigmath.es.osaka-u.ac.jp

EDUCATIONS/TRAINING

1978	University of Tokyo, Graduate School of Science, Japan, MD.
1981	Ph. D. (Doctor of Science), Tokyo University

POSITIONS

1978-1986	Research Associate, University of Tokyo, Faculty of Science, Japan
1986-1988	Lecturer, University of Tokyo, Faculty of Science, Japan
1988-1992	Associate Professor, Faculty of Science, Tokyo Metropolitan University, Japan
1993-1995	Professor, Ehime University, Faculty of Science, Japan
1995-2002	Professor, Osaka University, Graduate School of Science, Japan
2002-present	Professor, Osaka University, Graduate School of Engineering Science, Japan

RECENT PUBLICATIONS (less than 10 papers please)

1. Watanabe A, Hoshino D, Koshikawa N, Seiki M, Suzuki T and Ichikawa K. Critical role of transient activity of MT1-MMP for ECM degradation in invadopodia. ***PloS Computational Biology*** 9: e1003086, 2013.
2. Hoshino D, Nagano M, Koshikawa N, Suzuki T and Seiki M. The phosphoinositide-binding protein ZF21 regulates ECM degradation by invadopodia. ***PloS One*** 8: e50825, 2013.
3. Saitou T, Itano K, Hoshino D, Koshikawa N, Seiki M, Ichikawa K and Suzuki T. Control and inhibition analysis of complex formation processes. ***Theoretical Biology and Medical Modeling*** 9: 33, 2012.
4. Hoshino D, Koshikawa N, Quaranta V, Weaver V, Seiki M, Suzuki T and Ichikawa K. Establishment and validation of computational model for MT1-MMP dependent ECM degradation and intervention strategies. ***PLoS Computational Biology*** 8: e1002479, 2012.
5. Saitou T, Rouzimaimaiti M, Koshikawa N, Seiki M, Ichikawa K and Suzuki T. Mathematical modeling of invadopodia formation. ***J. Theoretical Biology*** 298: 138-146, 2012.
6. Suzuki T. Mathematical models of tumor growth systems. ***Mathematica Bohemica*** 137: 201-218, 2012.
7. Ichikawa K, Suzuki T and Murata N. Stochastic simulation of biological reactions, and its applications for studying actin polymerization. ***Physical Biology*** 7: 046010, 2010.