

A Mathematical Modelling of Signal Transduction System via Insulin Medication

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ABSTRACT

When insulin is injected to a cell, various signal transductions occur as a reaction. There are various molecular transducers such as Insulin Receptor (IR), Insulin Receptor Substrate (IRS), Protein Kinase B (PKB, also known as Akt), and Extracellular Signal-Regulated Kinase (ERK), etc., in a cell. These transducers are phosphorylated under some stimulation and then deliver information to other transducers. In this paper, we formulate a mathematical model for these physiological signal transduction phenomena via insulin medication and analyze this insulin signal kinetics using the phosphorylated transducers measured from the laboratorial experiments. It turns out that transfer rate from one transduction compartment to another depends on the quantity of the medicated insulin. Further, there is no reverse transfer action from the phosphorylated ERK to the regular ERK. Through this novel signal transduction model, it is possible to predict the reaction quantity of each transducer once the amount of the medicated insulin is known, which is very important to regulate the pharmaceutical uptake.

REFERENCES

1. Harvey J. Gold, *Mathematical Modelling of Biological Systems*, A Wiley-Interscience publication, 1977.
2. Jeremy M. Berg, John L. Tymoczko, Lubert Stryer, *Biochemistry*, 5th Edit, W. H. Freeman and Company, 2002.
3. John Penny and George Lindfield, *Numerical Methods Using MATLAB*, Prentice Hall, 1999.
4. D. Brown and P. Rothery, *Models in Biology: Mathematics, Statistics and Computing*, Wiley, 1993.
5. G. J. Borse, *Numerical Methods with MATLAB*, PWS Publishing Company, 1997.
6. H. J. Lee, K. K. Lim, S. H. Ha, B. D. Lee, K. I. Kim, P. G. Sub and S. H. Ryu, "Separate Kinetic Analysis of the Insulin Signal Transduction in HEK 293 cells", pre-print
7. C. S. Park, Ian C. Schneider and Jason M. Haugh, "Kinetic Analysis of Platelet-derived Growth Factor Receptor/Phosphoinositide 3-Kinase/Akt Signaling in Fibroblasts", *J. Biol. Chem.*, Vol. 278, 2003, pp.37064-37072.

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8. C. Taha, A.Klip, "The Insulin Signaling Pathway", *J. Membrane Biol.*, Vol. 169, 1999, pp.1-12.
9. Derek P. Brazil, J. S. Park and Brian A. Hemmings, "PKB Binding Proteins: Getting in on the Akt", *Cell*, Vol. 111, 2002, pp.293-303.
10. Gary L. Johnson and Razvan Lapadat, "Mitogen-Activated Protein Kinase Pathways Mediated by ERK, JNK, and p39 Protein Kinases", *SCIENCE*, Vol. 298, 2002, pp.1911-1912.
11. Hatakeyama M, Kimura S, Naka T, Kawasaki T, Yumoto N, Ichikawa M, Kim JH, Saito K, Saeki M, Shirouzu M, Yokoyama S, Konagaya A., "A computational model on the modulation of mitogen-activated protein kinase (MAPK) and Akt pathways in heregulin-induced ErbB signalling.", *Biochem J.*, Vol.373, 2003, pp451-463.
12. Nathalie A. Lokker ,James P. O'Hare ,Arpy Barsoumian , James E. Tomlinson ,Vanitha Ramakrishnan ,Larry J. Fretto andNeill A. Giese,"Functional Importance of Platelet-derived Growth Factor (PDGF) Receptor Extracellular Immunoglobulin-like Domains", *J. Biol. Chem.*, Vol. 272, 1997, pp. 33037-33044.
13. Sandra J. Watton and Julian Downward,"Akt/PKB localisation and 3 phosphoinositide generation at sites of epithelial cell-matrix and cell-cell interaction", *Current Biology*, Vol. 9, 1999, pp. 433-436.