# An Egf Signaling RoadMap in Pathway Logic

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***Short Abstract* — We present a Pathway Logic model of early signaling in mamalian adherent cells in repsonse to stimulation by epidermal growth factor (Egf).**

## I. Pathway Logic

Pathway Logic [1,2] is an approach to modeling cellular processes based on rewriting logic, a simple logic designed for modeling and analysis of distributed systems. It allows one to model aspects of the structure and state of interacting components as elements of an abstract data type; to represent individual process steps (reactions) as rewrite rules; and to study possible ways a system might evolve using techniques based on logical inference. Given a network of reactions and a specification of cellular components one can query the network about possible reaction pathways and outcomes. Knockouts that prevent a given outcome can be computed, competing reactions can be found, and pathways can be compared to look for potential cross-talk.

## II. EGF Signaling Model

Epidermal growth factor receptor (EgfR) signaling [3] regulates growth, survival, proliferation, and differentiation in mammalian cells. We present a Pathway Logic model of early response to Epidermal growth factor (Egf) stimulation in adherent cells expressing Egf-receptors. The model is entirely based on experimental results and data curated from the published scientific literature.

We explain how reactions are represented as rewrite rules, as well as the curation process that extracts information about state changes and biological context from experimental data to determine the components of a reaction rule. The resulting reaction network for EgfR signaling has over 370 reactions involving more than 460 species (signaling molecules in different states and locations). It includes all data supporting events that might be downstream of Egf. In addition, outcomes that have been demonstrated experimentally to happen in response to a short stimulus with Egf are represented as goals---states to be reached from an initial state by applying the reaction rules. So far more than 80 such outcomes have been collected and used to test the adequacy of the model---does it predict the observed outcomes? We will also point out some surprises that appear in the generated pathways due to the richness of the considered biological context.

## III. Conclusion

Pathway Logic models are qualitative and thus answer different kinds of questions than quantitative differential equation-based or stochastic models. They can also serve as useful road maps for developing quantitative models of subsystems and understanding the potential cross talk between signaling submodules.

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## References

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Acknowledgements: This work was funded by NIH/NIGMS grant GM68146 and the NIH/NIC ICBP program..

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