Novel small GTPase family exhibiting unique biochemical properties

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GTP-binding proteins, which cycle between the two different conformations of GTP- and GDP-bound states, play important roles as a "molecular switch" in many intracellular signaling pathways. There are several G protein families including trimeric G proteins, factors involved in protein synthesis and mRNA degradation, and small GTPases. The small GTPases, such as Ras, Rab, Arf, and Rho/Rac family, are involved in the regulation of cell growth and differentiation, intracellular vesicle trafficking, and cell shape and adhesion. However, there are still many other small GTPases, of which functions are unknown.

We have recently identified novel small GTPases exhibiting unique biochemical properties and tissue expression. Di-Ras, which belongs to a distinct branch of the Ras family, had only a quite low level of GTPase activity and existed predominantly as a GTP-bound form in living cells. The expression of Di-Ras was rather specific in neuronal cells, and its over-expression induced apoptotic cell death with DNA fragmentation, which was inhibited by caspase inhibitors. Interestingly, Di-Ras did not induce apoptosis in non-neuronal cells, suggesting that Di-Ras-mediated apoptosis is only activated in neuronal cells. In addition, we also identified the small GTPase Gie, which stands for novel GTPases indispensable for equal segregation of chromosomes. Although Gie is now classified into Arf family and named as Arl8, Gie forms a distinct subfamily of Arf in terms of the lack of N-terminal myristoylation motif conserved in other Arf family members. In this symposium, we would like to present the recent research progress on these atypical small GTPases.