'97中国青年学者生物学学术讨论会

生物膜研究的前沿

DEC.22–26

中　国　科　学　院

国家自然科学基金委员会

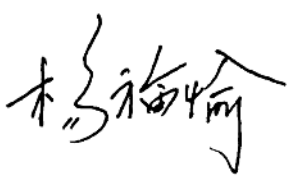
前　言

我国科学家在50年代即已开始对琥珀酸脱氢酶及线粒体的氧化磷酸化、叶绿体的光合磷酸化进行了卓有成效的研究并获得了优异的成果，引起了国际同行的广泛注意。遗憾的是十年动乱中断了这方面的研究。文革以后，我国生物膜研究才得以复兴并得到了比较全面的发展。从1981年开始，在中国科学院的支持下，中国生物化学学会、中国生物物理学会和中国细胞生物学学会联合召开了首届全国生物膜学术讨论会，以后每三年举行一次，迄今已连续举办了六次。1984年，在国际生化学会、国际生物物理学会生物能力学小组和中国科学院的支持下，在北京还组织了一次<国际生物膜与生物能力学学术讨论会>。总之，经过在艰苦条件下的努力奋斗，我国生物膜研究从无到有，从小到大，无论从广度到深度都已发生了明显的变化，但与国际先进水平相比较，从整体上仍然存在着差距。

在中国科学院与国家自然科学基金会的支持下，我们组织了以《生物膜研究的前沿》为专题的青年学术讨论会，它使国内外从事生物膜科研的华裔生物膜青年专家有机会欢聚一堂。他们有的是在美国、加拿大、德国、瑞士、

中国香港等国家和地区工作或学习的生物膜科技工作者，也有来自北京、上海、天津、沈阳、长春、哈尔滨、广州、重庆、成都、武汉等城市的青年学者。此外，我们还特邀部分我国老一辈生物膜专家参加这一盛会，与会总人数近百人。在这次会上，大家不仅可以共叙友情，促进了解，也可以交流切磋，共同提高。相信通过这次会议，不仅能促进今后我国生物膜研究的发展，甚至也有可能会影响即将来临的二十一世纪中国生物膜的研究。

祝会议开得生动活泼，圆满成功！



教授

会议名誉主席

中国科学院院士

一九九七年十二月二十二日

'97中国青年学者生物学学术讨论会
《生物膜研究的前沿》专题讨论会

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致谢:

《生物膜研究的前沿》学术讨论会组委会衷心感谢中国科学院生物物理研究所，美国贝克曼仪器公司(北京)对此会议的支持.

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论文摘要集

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论 文 目 录

专题 A 信号跨膜转导 细胞凋亡

专题 B　离子通道　物质跨膜运输

专题 C 三类ATP酶 光合膜蛋白

专题 D 膜脂－膜蛋白相互作用

专题 E　膜蛋白结构　新技术和方法

Signal Roles of PI 3-Kinase in G Protein Coupled Receptor Stimulation of Mitogenesis

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Phosphoinositide 3-kinase (PI 3-kinase) is a key signaling enzyme implicated in the regulation of a broad array of biological responses such as membrane receptor-mediated mitogenesis, antiapoptosis, oxidative burst, membrane ruffling, and glucose uptake. The activation of PI 3-kinase results in an increase in cellular levels of D-3 phosphorylated phosphoinositides, such as PtdIns(3)P, PtdIns(3,4)P2, and PtdIns(3,4,5)P3. These products, however, do not serve as the substrates of phospholipase C and thus have been proposed to act as second messengers. In this regard, recent studies have indicated that PtdIns(3,4)P2 can directly activate certain protein kinase C and Akt and PtdIns(3,4,5)P3 is capable of binding to the Pleckstrin homology domain of guanine nucleotide exchange factor of the small GTP-binding protein ARF 1.

Multiple forms of PI 3-kinase with distinct mechanisms of regulation and different substrate specificity have been discovered. PI 3-kineses are divided into two main classes. The first class has substrate specificity restricted to phosphatidylinositols (PtdIns); their function is not clear. The second class of PI 3-kineses, in addition to PtdIns, can also utilize PtdIns(4)P and PtdIns(4, 5)P2 as substrates. This class of PI 3-kinase has been further clarified into two subgroups according to their preference for adaptor proteins in the cellular signaling events. The first subgroup PI 3-kinase is a heterodimer consisting of a p85 adaptor protein and a p110 catalytic subunit. The cDNAs of four related p85 subunits and two related p110 subunits (α and β) have been identified. The N-terminus of p110 has docking sites for p85 subunit and oncoprotein Ras; the C-terminus contains the core kinase domain. The p85 subunit is

characterized by containing a variety of domain modules for protein-protein interactions. These include an N-terminal SH3 domain, two SH2 domains (N- and C-SH2) separated by the inter-SH2 region (iSH2); and two proline rich regions. The two SH2 domains bind tyrosine-phosphorylated receptors and in this manner recruit the p85-p110 complex to activated receptors. The iSH2 region mediates the interaction of p85 and p110 which is essential for catalytic action of p110. This subgroup is mainly stimulated by membrane-bound receptors activating tyrosine kinase. Stimulation of tyrosine kinase receptors by extracellular signals phosphorylates specific tyrosine residues located in the YMXM motifs of their own receptors or adaptor molecules, such as insulin receptor substrate-1. These phosphorylated proteins bind to the SH2 domains of p85 and stimulate the lipid kinase activity. The stimulatory effect of these proteins can thus be mimicked in vitro by a synthetic tyrosine-phosphorylated peptide possessing the YMXM motif .

The second subgroup of PI 3-kinase using multiple phosphorylated inositol lipids as substrates are those that do not bind p85 adaptor proteins. Instead, their catalytic subunits of approximately 110-120 (also termed p110 γ) kDa seem to depend on a p101 subunit. This group of PI 3-kinase has been thought to be only activated by heterotrimeric G protein subunits (α and/or βγ subunits). Indeed, a novel catalytic subunit of PI 3-kinase, designated as p110, has been cloned and shown to be activated in vitro by both the α and βγ subunits of G proteins. This isozyme lacks the binding site to p85 and thus does not interact with the regulatory subunit. Additionally, Stephens et al. recently reported a heterodimeric PI 3-kinase consisting of a p110-related 120-kDa catalytic subunit and a 101-kDa adaptor protein, which is distinct from p85. PI 3-kinase activity of the novel heterodimer was markedly stimulated by G but not by a tyrosine-phosphorylated peptide.

In contrast to these reports, several authors including us have demonstrated that G protein coupled receptor is capable of stimulating PI 3-kinase activity immunoprecipitated with anti-p85 antibodies. For example, insulin-induced accumulation of PtdIns(3,4,5)P3 in THP-1 cells is synergistically enhanced by activation of a pertussis toxin-sensitive G protein, suggesting that this isozyme is regulated by both