轴突生长导向信号的网络特征分析

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轴突定向生长是实现神经元之间准确连接的关键步骤,其导向机制是一个远未完全解开的谜团。本文以京都基因和基因组百科全书数据库(KEGG)所提供的轴突导向分子家族主要成员(netrins, slits, semaphorins 和 ephrins)之间的信号传递关系为依据,将信号及其关联分别处理成结点和连线,借助 VisANT 软件(Intergrative Visual Analysis Tool for Biological Networks and Pathways)构建轴突生长导向信号的网络模型,着重进行网络特征分析。研究结果表明,轴突生长导向信号网络具有无标度网络属性,即在众多的结点(信号分子)中只有为数不多的几个为重要结点(重要信号分子)、有较多的信号转导分子或作用底物与它们直接连接,而网络中大多数结点为次要结点、只有少数其它结点与之发生直接连接。本文的工作为鉴别轴突定向生长过程中的关键导向分子提供了有效途径。

微重力细胞生物学实验地面模拟技术研究

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微重力对细胞的影响是空间生命科学研究的重要环节,(哺乳动物)细胞感受重力变化的机制是其中的一个基本问题。由于空间实验机会稀少且成本昂贵,必须辅助以相关的地面微重力效应模拟方法。旋转培养器在微重力细胞生物学实验中一直是模拟微重力效应的主要手段,其前提假设是,旋转可以"迷惑"细胞对固定重力方向的感知,并且重力方向改变的速度快于细胞对重力方向感知的响应时间阈值。严格上说旋转培养器并不能"模拟"微重力,但可能模拟微重力的部分效应,主要是细胞对重力矢量方向紊乱的响应。微重力细胞生物学实验一直面临如何将浮力对流消失引起的细胞培养传质条件改变的影响与细胞对重力的直接感应有效区分开来的问题。旋转培养器的实验条件是否能够与常规细胞培养条件以及空间实验条件进行对照对于分析真实的细胞重力感应机制至关重要[1,2,3]。现有的各类旋转培养器(以转壁式培养器为代表)均未能很好地解决这一问题。为此,针对贴壁依赖性细胞和非贴壁依赖性细胞(悬浮培养细胞)两种培养形式,本研究提出了旋转扁平流动腔培养器和片流逆流式旋转培养器两种新的地面模拟实验技术。分析了两类培养器的培养室内流场特征(主要考查流速分布以及流动剪切)、物质交换(主要是气体交换与葡萄糖代谢)效率。此外,对旋转产生的离心力的影响进行了分析。在上述基础上,开发了可以对培养条件(主要是温度、ph 值及气压)实时监控的配套实验系统。研究表明,旋转扁平流动腔培养器适合于贴壁依赖性细胞培养,其培养腔室结构简单(扁平矩形片状),培养基底范围内流场均匀,流动剪切可控。经气液循环装置确保氧供应的情况下,可满足其它物质交换要求。在对培养面积要求不是很大的情况下($<8\ cm^2$),对于 15 rpm 的转速条件,可以将离心力降低至 $10\text{-}3\times g$ 水平而避免附加"人为的重力"干扰。通过改变旋转半径和转速,可以用于模拟不同水平的重力条件(包括常重力和超重力)。该培养器还具有体积小,重量轻的特点,因而节约资源,便于改造成为空间实验中的 $1\times g$ 对照装置。上述特点均可弥补利用微载体在转壁式培养器中进行贴壁依赖性细胞培养这一实验手段存在的内部流场复杂,无法进行不同重力条件下对照[1,2]等不足。片流逆流式旋转培养器适合于非贴壁依赖性细胞培养,其结构利用两层可以通过培养液但不能通过细胞的薄膜将培养腔室分隔成为三部分,上下两侧为灌注流道,两层薄膜间为细胞培养室。两侧流道内的培养液分

别从相反方向灌注,并通过薄膜向细胞培养室内缓慢渗流,从而达到促进物质交换和细胞的均匀分布,降低流动剪切的目的。在对培养容积要求不是很大的情况下(<3 ml),对于 15 rpm 的转速条件,该培养器也可以将离心力降低至 $10^{-3}\times g$ 的水平,并可以消除转壁式培养器在地面和空间实验中分别需要利用内外筒同速旋转和差速旋转两种实验条件[1]的缺陷。使用局部温控装置、光电 pH 传感器以及压力传感器通过自动控制程序监控,可以对上述培养器的实验条件得到实时控制和记录。上述实验技术将为促进微重力细胞生物学研究,揭示细胞响应重力变化的机制提供有效的研究手段。(国家自然科学基金项目 30870601/30730032/30730093,中国科学院知识创新工程项目 KJCX2-YW-L08),科技部国家重大研究计划 2006CB910303 和科技部 863 项目 2007AA02Z306。)

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Dynamics of the HBV model with diffusion and time delay

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Chronic hepatitis B infection is a major health problem, with approximately 350 million virus carriers worldwide. In Africa, about 30%-60% of children and 60%-100% of adults have been infected with hepatitis B virus (HBV). Persistent infection with HBV can lead to cirrhosis and primary hepatocellular carcinoma. Mathematical models are a useful tool to forecast the future development of diseases. In 1981, Capasso and Maddalena proposed and analyzed a reaction diffusion system modeling the spatial spread of a class of bacterial and viral diseases. Gardner and the monographs by Fife, Britton, Murray, and Volpert et al. proposed reaction-diffusion equations and their applications to biology for the case without time delay, and Wu and Schaaf for the case with time delay. In 1996, Nowak and Charles introduced population model into dynamics of virus, provided nonintuitive insights into the dynamics of host responses to infectious agents. This model is widely applied to evaluate the anti-HIV agents therapeutic effectiveness.

The use of interferon or nucleoside analogs such as lamivudine, entecavir and adefovir dipivoxil can partially inhibit the replication of HBV, however, HBV could not be entirely eradicated due to persistence of viral replication. Additionally, adverse effects, escape mutants and recurrence are often observed following long-term treatments and drug withdrawal. Therefore, the evaluation and investigation of novel strategies to treat this disease are necessary and urgent. Based on the medical and biological research results, the mathematical model is established to reflect the interaction between HBV and HBV drugs. It can help us to understand the mutual effect between HBV and HBV drugs and to assessment the curative effect of HBV drugs. Consequently, HBV drug screening can be sped up and corresponding measures can be taken to prevent and cure HBV infection. Based on the mechanism of HBV infection, a HBV Model referring treatment with diffusion and time delay was studied in this paper. The immune system can recognize the viral antigens but can not effectively control viral replication. Therefore, the artificial injection of medicine is a valid method of HBV control, which can suppress virus replication. The identification of carriers at risk is the first step in preventing progressive liver disease and avoiding non-appropriate treatments. A better answer for personalized antiviral therapy may come from the combined use of molecular biology and bio-mathematical modeling that can help medical doctors to give appropriate cure scheme according to the dynamic of viral infection during therapy. For HBV infection, susceptible host cells and infected cells are hepatocyte, so cannot move under normal conditions, but viruses can move freely in liver. Medication can also diffuse in liver. Motivated by these observations and based on the well-studied Fisher equation and some biological assumptions, the model of HBV infection with spatial dependence is proposed. We will show under some mild conditions, that the e-