Analysis of unique and specific genetic markers for diagnosis of antibiotic resistant, pathogenic escherichia coli (E. coli) encoding resistance to the third generation antibiotic, cefotaxime

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Abstract

Among the wide range of antibiotic available, beta-lactam antibiotics are used widely in bacterial pathogenic infections. The most common cause of bacterial resistance against beta-lactam antibiotics is the production of beta-lactamases by many members of Enterobacteriaceae family, including especially, E. col. (Harwalkar, Sataraddi et al. 2013). Extended-spectrum Î²-lactamases (ESBLs) are resistant to the third generation antibiotics, cephaloosporins and monobactum, additionally, these ESBL producing organismsâ ™ exibit co-resistant to many other classes of antibiotics resulting limited treatment alternatives (Paterson, Bonomo 2005, Lartigue, Zinsius et al. 2007, Lewis, Herrera et al. 2007). Over the past decade, it has been observed dramatic increase of these ESBL producing E. coli strains, especially, CTX-M family of ESBL producers, to the third-generation cephalosporin antibiotic, Cefotaxime (Bonnet 2004, Lartigue, Zinsius et al. 2007, Paterson, Hujer et al. 2003, Paterson, Bonomo 2005, Ruppe, Lixandru et al. 2013). Although studies have published the diagnosis of various ESBL producers in worldwide, only few reports of molecular identification of CTX-M family of genes have been published (Al-Mayahie 2013, Harwalkar, Sataraddi et al. 2013, Literacka, Bedenic et al. 2009). This study aims to identify the DNA segments of CTX-M genes unique to E. coli, and analyse the surrounding genetic makeup of CTX-M genes. Collectively, understanding the genetic makeup of these resistance genes will shed a light on their mechanistic of antimicrobial resistance. Unlike other conventional clinical diagnostic methods, molecular diagnostics seeks evidence of a disease at the very basic causative level by detecting the nucleic acid identity. The main advantage of this diagnostic method is that the diagnosis carried out in the molecular level, and the method will identify the microbial pathogens at the early stages of the infectious diseases (Versalovic, Lupski 2002). Different types of rapid detection systems such as Real-Time PCR have been used to identify the different CTX-M family target genes (Birkett, Ludlam et al. 2007, Li, Chen 2012, Versalovic, Lupski 2002, Woodford, Fagan et al. 2006, Woodford, Sundsfjord 2005). The identified genes so far, has some degree of potency for identification, but the majority of these genes lacks the characteristics of a strong and unique genetic marker that can used as a specific target solely for identification of any CTX-M family of ESBL producing E. coli strains. Therefore this study analyse short DNA segments and develop a sensitive, specific and reliable method that can be used for rapid selective detection of ESBL producers resistant to Cefotaxime in antibiotic resistant E. coli strains.

http://dx.doi.org/10.1016/j.nhtm.2014.11.051

Luminescent dual sensors reveal extracellular pH-gradients and hypoxia on chronic wounds that disrupt epidermal repair

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Abstract

Wound repair is a quiescent mechanism to restore barriers in multicellular organisms upon injury. In chronic wounds, however, this program prematurely stalls. It is known that patterns of extracellular signals within the wound fluid are crucial to healing. Extracellular pH (pHe) is precisely regulated and potentially important in signaling within wounds due to its diverse cellular effects. Additionally, sufficient oxygenation is a prerequisite for cell proliferation and protein synthesis during tissue repair. It was, however, impossible to study these parameters in vivo due to the lack of imaging tools. Here, we present luminescent biocompatible sensor foils for dual imaging of pHe and oxygenation in vivo. To visualize pHe and oxygen, we used time-domain dual lifetime referencing (tdDLR) and luminescence lifetime imaging (LLI), respectively. With these dual sensors, we discovered centripetally increasing pHe-gradients on human chronic wound surfaces. In a therapeutic approach, we identify pHe-gradients as pivotal governors of cell proliferation and migration, and show that these pHe-gradients disrupt epidermal barrier repair, thus wound closure. Parallel oxygen imaging also revealed marked hypoxia, albeit with no correlating oxygen partial pressure (pO2)-gradient. This highlights the distinct role of pHe-gradients in perturbed healing. We also found that pHe-gradients on chronic wounds of humans are predominantly generated via centrifugally increasing pHe-regulatory Na+/H+-exchanger-1 (NHE1)-expression. We show that the modification of pHe on chronic wound surfaces poses a promising strategy to improve healing. The study has broad implications for cell science where spatial pHe-variations play key roles, e.g. in tumor growth. Furthermore, the novel dual sensors presented herein can be used to visualize pHe and oxygenation in various biomedical fields.

http://dx.doi.org/10.1016/j.nhtm.2014.11.052

Integrated testing strategy of pharmaceutical intermediates for occupational health

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Abstract

In order to assess the occupational health hazard of intermediates (IM), hazard data were traditionally generated through experimental animal testing, which are more and more replaced by alternative methods considering animal welfare and costs. Indeed, there are a number of other ways to assess the health hazards: comparing substances with similar structures, grouping them together into logical categories, doing specialized computer modelling, using weight of evidence approach (WoE) and integrated testing strategy (ITS). We have evaluated the current state of scientific knowledge from the literature and from in silico evaluation tools. We have proposed new ITS for Novartis Pharma own pharmaceutical IM for occupational health purposes which defines the tiered approach in performing in silico, in vitro and in vivo studies which support risk management to prevent workplace diseases that could be triggered by IM and reduces the number of in vivo tests required.

http://dx.doi.org/10.1016/j.nhtm.2014.11.053

Bilateral wrist robot-assisted training in chronic hemiplegic stroke: A pilot study

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Abstract

Background: The stroke population needing physical rehabilitation of the upper extremity is constantly increasing. To solve this problem, robot devices for improving motor performance are developed to assist physical rehabilitation in Korea. The aim of this study was to develop the robot-assisted wrist training system and to apply this to the chronic hemiplegic stroke participants.

Methods: Bilateral wrist robotic device was developed and we applied this to four chronic hemiplegic stroke participants. Robot-assisted wrist