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Oridonin: A novel inhibitor of SpeB regulates virulence in *Streptococcus pyogenes*

Haiqing Yu, Nan Wang, Hong Yu, Qiong Hong and Hongmin Sun
University of Missouri, USA

Streptococcus pyogenes is a common clinical pathogenic bacterium and 1800 invasive *S. pyogenes* disease-related deaths are reported in the USA yearly; among which, streptococcal toxic shock syndrome has a mortality rate of 30-70%. Pharmacological studies showed that Oridonin, a natural product of *Rabdosia rubescens* herb, has antimicrobial activities. However, the underlying mechanism of Oridonin in blocking *Streptococcus pyogenes* is still obscure. In the current study, *Streptococcus pyogenes* strain ATCC 19615 (serotypes 5 and 49) was treated with 50 μ M Oridonin for 20 hours and the secretion proteins with differential expression were identified and analyzed by SDS-PAGE and LC-MS/MS, respectively. The expression level of differential gene was analyzed via using quantitative RT-PCR (qRT-PCR) and western blot. Based on an intraperitoneal injection mouse model with $6-8 \times 10^9$ CFU, the virulence of *S. pyogenes* was investigated between DMSO group and Oridonin group by counting the CFU in spleen. The results indicated that (1) SDS-PAGE and LC-MS/MS analysis indicated that SpeB (Streptococcal Pyrogenic Exotoxin B) was significantly decreased in Oridonin group ($p < 0.01$). (2) qRT-PCR data showed that the transcriptional levels of SpeB, LuxS (activator), LacD1 (repressor) and Eno (chaperone) were dramatically decreased ($p < 0.01$). The western blot analysis indicated that the maturation and processing of SpeB were blocked by Oridonin ($p < 0.01$). (3) The spleen CFU of *S. pyogenes* were reduced in Oridonin group ($p < 0.05$). Our result suggests that Oridonin is a novel inhibitor of SpeB and it regulates virulence in *Streptococcus pyogenes*.

YUHA@HEALTH.MISSOURI.EDU

Leprosy classification methods: A comparative study in a referral center in Brazil

Ismael Alves Rodrigues Junior and Rosa Maria Esteves Arantes
Universidade Federal de Minas Gerais, Brazil

We first faced particularities of leprosy classification methods while working on the correlation between the degree of thermal sensitivity impairment of leprosy cutaneous lesions, measured by quantitative sensory test and the degree of lesions denervation, evaluated by immunohistochemistry anti-PGP 9.5. WHO operational classification (WOC) differentiates patients in paucibacillary (up to five skin lesions) and multibacillary (six or more lesions) and is the one used in the field. The Ridley and Jopling classification (RJC) differentiates patients according to their clinical, histopathological, bacteriological and immunological presentation and is the most widely used scientific classification. Different authors have pointed out that many multibacillary RJC patients are misclassified as paucibacillary by WOC. This may result in inadequate treatment duration, underestimation of the sequelae risk and difficulty for the epidemiological control. On the other hand, different authors have shown considerable disagreement between RJC clinical and histological components. In consonance with the literature, our data showed that WOC overestimated the number of multibacillary patients (42.9% vs. 36.8%) but also classified as paucibacillary 28.6% of the RJC multibacillary patients. The slit-skin smear bacilloscopy, currently out of 'WHO' recommendations, reclassified as multibacillary 14.8% of the WOC paucibacillary patients and as paucibacillary 42.8% of the WOC multibacillary patients. As for the clinical and histopathological components of RJC, the agreement was perfect in 46.9% of the sample. The most delicate aspects were the histopathological differentiation between the tuberculoid and borderline-tuberculoid forms and the histopathological classification of the mid-borderline form. It seems that these issues arise from RJC histopathological criteria flaws.

ismaelalvesrodrigues@gmail.com