The genomic basis for the variable biochemical profiles that lead to erroneous identifications of emerging pathogenic *Corynebacterium spp*.

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Emerging and reemerging pathogenic bacteria of the genus Corynebacterium have been increasingly recognized as the causative agents of infections in humans. The identification of these bacteria by the most commonly used phenotypic tests, based on batteries of twenty-one biochemical reactions, is considered as challenging, and normally requires additional methods including 16S rRNA gene sequencing and MALDI-TOF mass spectrometry. In particular, the frequently reported species C. amycolatum, C. striatum, C. xerosis and C. minutissimum (XSMA group) normally generate biochemical profiles that may lead to ambiguous and even erroneous identifications in the clinical microbiology laboratory. Besides, the most frequently found species C. diphtheria, which causes the reemerging disease diphtheria, may present a variable carbohydrate fermentation profile, then hampering appropriate identification by commonly used biochemical methods. In order to study the genetic basis for the variable profiles observed for these bacteria in biochemical tests, we performed a comparative genomic analysis between 13 strains of C. diphtheria and between several isolates of bacteria of the XSMA group. Various reactions and metabolic pathways that show variability in biochemical tests were targeted in this work, including: sucrose, galactose, maltose, ribose and glycogen utilization, and nitrate reduction. The enzyme codes for each of metabolic reactions were obtained from MetaCyc database and used to obtain the sequences of proteins in the UniProt database. TBLASTN searches were performed using the following cut-off parameters: 70% query cover, 30% identity and expect value < 10-4. Among the C. diphtheria strains it was identified a lineage-specific presence of sucrose degradation pathway, this result provides evidence of the biochemical plasticity observed in this species, since the literature indicates as sucrose non-fermenting bacteria. Some genes necessary for the maintenance of the metabolic pathway were identified in genomic islands present in strains of C. diphtheria 31A and BH8, this is a major finding to account for the typically observed variability. The proteins necessary for maintenance of the pathway of degradation of sucrose were modeled and aligned with corresponding proteins of C. glutamicum, a species presenting sucrose utilization capacity, and showed high similarity. The biochemical variability of the XSMA group, observed in the literature for these reactions were confirmed by genomic analysis in silico.