Bioinformatics, including data management

T001

CARBAPENEM RESISTANCE PREDICTION BY BACTERIAL GENOME-WIDE-ASSOCIATION-STUDY IN NON-FERMENTING BACILLI: PSEUDOMONAS AERUGINOSA AND ACINETOBACTER BAUMANNII.

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BACKGROUND-AIM

Antimicrobial resistance (AMR) (or drug resistance) is a natural phenomenon where microorganisms change their molecular, physical, or chemical structures to resist the drugs created by infections. The World Health Organization (WHO) had released for the first time a list of Multidrug-Resistant Bacteria (MRB) that pose the greatest threat to human health and for which new antibiotics are desperately needed. Acinetobacter baumannii and Pseudomonas aeruginosa resistant to carbapenems are part of the Gram-negative non-fermenting bacilli group with critical priority according to the WHO. For this, the final research purpose was to create and train a bioinformatic study capable of finding critical k-mers that could differentiate those strains of P. aeruginosa and A. baumannii resistant to carbapenems.

METHODS

Four k-mers sizes were performed for each bacterium (12, 14, 16, and 18), and two training and testing (30:70 and 20:80) schemas were used over seven different machine learning algorithms: Random Forrest, Adaboost, Xgboost, Decision Trees, Bagging Classifier, Support Vector Machine, and KNN. For both bacteria, the best models were obtained when using a k-mer length of 12. In the case of Acinetobacter baumannii, the best models obtained an accuracy of 0.99 for testing.

RESULTS

Moreover, for Pseudomonas aeruginosa, the best accuracy obtained was 0.93 when us- ing Bagging Classifier. To investigate the sequences of the k-mers obtained, the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool BLAST was used. Ten to twenty sequences built with the k-mers were investigated for each model. When using a k-mer length of 12 for A. baumannii, 18 out of 20 sequences represented a crucial sequence in antibiotic resistance. In the case of P. aeruginosa, 16 out of 20 sequences represented a key sequence. To complement this research, a Dynamic Programming algorithm was used to find changes over the reference genome that could explain the resistance within the resistant genomes. Not all the resistant k-mer sequences were found over the reference genome, as some of them could be acquired by horizontal transference (Conjugation, Transformation, or Transduction inheritance).

CONCLUSIONS

Further investigation over these sequences can be applied in creating new directed antibiotics or detecting easily resistant strains of Pseudomonas aeruginosa or Acinetobacter baumannii resistant to carbapenems.

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T002

THE Y CHROMOSOME, AN IMPACT ON HUMAN LONGEVITY?

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BACKGROUND-AIM

Life expectancy at birth is higher for women (46,XX) than for men (46,XY): 74.2 years vs 69.8 worldwide in 2016 according to the World Health Organization. Moreover, the longevity of 47,XYY patients is reduced by 10 years compared to 46,XY subjects whereas it is reduced by only 2.1 years in 47,XXY patients compared to 46,XY subjects. These data suggest a potential role of the Y chromosome in longevity. The aim was to test the hypothesis of the role of the Y chromosome in human longevity through its action on gene expression.

METHODS

A whole-transcriptome analysis (Illumina technologies) was performed on 25 subjects divided into 4 groups according to the number of gonosomes X and Y in the karyotype: XYY (n=4), XXY (n=9), XY (n=6) and XX (n=6). Then, a differential gene expression analysis (DESeq2 package) and an ontology analysis (gprofiler2 package) were realized with the R software.

RESULTS

The gene expression analysis showed the formation of clusters of subjects according to their karyotype. We noticed 5.65% of differentially expressed genes in the XYY vs XX comparison, 5.82% in the XXY vs XX comparison, 0.21% in the XY vs XX comparison, 0.17% in the XYY vs XY comparison, 0.26% in the XXY vs XY comparison, and 0.25% in the XYY vs XXY comparison. The differentially expressed genes identified were gonosomal genes but also autosomal genes. Among the overexpressed genes, an ontology analysis showed an enrichment for those involved in senescence and/or cell cycle processes for the XYY vs XX and XYY vs XXY comparisons.

CONCLUSIONS

These preliminary results indicated that the presence of the Y chromosome could modified autosomal gene expression and tended to induce an overexpression of genes involved in the senescence and cell cycle processes. This latter point may be linked to cancerous pathologies and tissue aging which was in favor of a potential deleterious effect of the Y chromosome on human longevity. These results are consistent with a previous study in Drosophila that showed longevity was inversely correlated with the number of Y chromosomes in the karyotype.

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T003

EVALUATION OF THE ICTERIC INDEX FOR THE MANAGEMENT OF THE DEMAND OF TOTAL BILIRUBIN USING BIG DATA

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BACKGROUND-AIM

The icteric index (IC) is an indirect assessment of the total bilirubin (TB) level in a sample. This index is performed in most requests received in the laboratory to detect analytical interferences and could be used to screen for pathological TB, as well as to manage the demand for this test.

METHODS

Retrospective study in which 434,125 requests with TB and IC performed, during 2020 in our hospital, on Cobas 8000 equipment (Roche Diagnostics) were extracted from a Big Data repository. The correlation coefficient and linear regression between both tests were evaluated. In addition, categorizing the variables, a contingency table was elaborated where a Chi-square test was applied. Finally, a ROC curve was performed to establish the cut-off point at which the IC can predict elevated TB (>1.2 mg/dL).

RESULTS

The two tests have a positive correlation coefficient of 0.97. The regression equation relating both tests is: TB=-0.21+0.76*IC.

In the contingency table, 99.9% of the samples with IC \leq 1 have normal TB. 55% with IC=2 have normal TB and 98.3% with IC>2 have elevated TB. The chi-square test between the three categories presents a p<0.0001.

The IC as a predictor of elevated TB had an AUC on the ROC curve of 0.981. The cut-off of IC>1 presents a Sensitivity of 98.76%, Specificity of 95.36%, a Negative Predictive Value (NPV) of 99.9% and a Positive Predictive Value (PPV) of 59.2%. The cut-off of IC>2 has a PPV of 98.3%.

On the one hand, by applying the IC as screening, we would avoid performing 383,321 TB (88.3%), which would result in an annual saving between earrow19,166 - earrow383,321 depending on the laboratory. On the other hand, in 2020, 6,614 requests were found without TB requested with IC>1, so performing TB in these samples could detect unknown elevated TB in more than half of these patients.

CONCLUSIONS

The IC can be used to screen for high TB by applying a cut-off of IC>1. This would make it possible to adjust the demand by performing only 11.70% of the TB requested with hardly any decrease in diagnostic yield. In addition, TB could be reflected in those requests with IC>1, which would improve the detection of occult hyperbilirubinemia.

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