

Directed acyclic graphs for phenotypes and genotypes association between oral mucosa and rat submandibular gland tumorigenesis

Mabel Brunotto¹, Ana M Zarate¹, José Luis Barra², Alicia Malberti¹

¹Departamento de Biología Bucal. Facultad de Odontología. Universidad Nacional de Córdoba.

²Centro de Investigaciones en Química Biológica de Córdoba (CIQUIBIC, UNC-CONICET), Departamento de Química Biológica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba

In recent years, the success of statistics in the field of genetics is to identify genes that affect the disease process, firstly developing models that respond to diseases Mendelian inheritance. However, the majority of diseases present complex etiology; cancer is an example. Within the head and neck cancers, the cancer of submandibular gland is detected in late stages and has the bad prognosis of survival. The experimental models using animals allow studying the developing of tumor at early times. However, it is impossible to measure variables such as saliva total; while it is possible the taking of saliva sample by salivary conduct, but this is not a useful methodology to screening programs that could be implemented for human population. The Directed Acyclic Graphs, which are a popular probabilistic tool for analyze and visualize conditional independence relationships from observed or unobserved –latent- variables are useful by understanding of complex diseases. Therefore the objective of this study was to apply the DAG models to assess the association between the observed phenotypic changes in rat oral mucosa and induced tumorigenesis in submandibular gland. We studied changes in oncogenes TP53 and bcl-2, histopathological and immunomarkers variables. It was used R package *ggm* for fitting Gaussian Graphical Markov models based on DAG. A set of linear structural equations was defined; and each formula indicates the response variables and the direct influences. The graph models indicated that there is an established relationship between the sequence alteration of gene bcl-2 in the submandibular gland and histological changes observed in the oral mucosa. In some of these tumours, overexpression of Bcl-2 was associated to bad prognosis coupled to other parameters such as localization, differentiation of the primary tumour and histological type. In consequence, this result associated with other clinical parameters could be useful to detect early changes of the submandibular gland tumorigenesis.