

## **Genomics and proteomics offers new hopes towards a personalized approach to lung cancer prevention and treatment**

**Lionel Gil\***

Programa de Biología Molecular y Celular  
Facultad de Medicina  
Universidad de Chile  
Santiago, Chile  
Tel: 56 2 6786068  
Fax: 56 2 7376320  
E-mail: lgil@machi.med.uchile.cl

**Marta Adonis**

Programa de Biología Molecular y Celular  
Facultad de Medicina  
Universidad de Chile  
Santiago, Chile  
Tel: 56 2 6786068  
Fax: 56 2 7356373  
E-mail: madonis@canela.med.uchile.cl

Cancer involves a pathological breakdown in the cellular process that control proliferation, differentiation and death of particular cells. World wide approximately 10 million people are diagnosed with cancer annually and more than 6 million die of the disease every year, over 22 million people in the world are cancer patients. In the period 1990-2000 an increase of around 19% in incidence and 18% in mortality has been observed. It is expected by 2020 that the number of cancer cases will double to 20 millions with an annual death of 12 millions. According to the World Health Organization, lung cancer is the most common malignant disease worldwide particularly among men, representing 12.3% of all cancers. It is the major cause of death from cancer, accounts for 1.1 million deaths a year and 17.8% of all cancer deaths, thus, represents the type of cancer with worse prognosis. No effective treatment is available for lung cancer; the five year survival rate for lung cancer patients is less than 15%.

### **RISK FACTORS**

It is estimated that at least 75% of the cancers are caused by chemical compounds in a process call chemical carcinogenesis. Lung cancer is generally a consequence of chronic exposure over long period of time to environmental carcinogen mixtures as well as other environmental, life style, diet and host factors. Environmental factors include air, water and soil air pollution, occupational exposures. Host factor include: genetic pattern, carcinogen exposure, carcinogen metabolism, DNA repair activity, oncogene and tumour suppressor expression and nutritional status.

Arsenic in drinking water in several areas of the world, as

in the II Region of Chile, has been related to increased risk of lung cancer and other cancers such as bladder and skin. Tobacco smoking is the main known cause of cancer related death worldwide. In the USA, Japan and Europe smoking accounts by 83-92% in men and 57-80% in women of the lung cancer deaths. The risk of lung cancer among smokers relative to the risk of non smokers is in the order of 8-15 in men and 2-10 in women. Many occupations and some specific chemicals encountered at work are associated with increase of cancer risk especially in newly- industrialized countries where most industrial activity take place in multiple small scale operations.

Outdoor and indoor pollution are also risk factors for lung cancer. Very high lung cancer rates occur in some regions of China and other Asian countries among non smoking women suggesting that indoor pollution as a result of combustions sources for heating and cooking is also a risk factor. Lung cancers is also attributable to outdoor air pollution, several studies have compared residence in urban vs. rural areas as a risk factor. In general lung cancer rates were higher in urban areas and correlate well with levels of respirable particulate matter as well as with specific pollutants such as polycyclic aromatic hydrocarbons (PAHs) or with mutagenic extracts in bacterial assay systems (Adonis et al. 1993).

A recent study done in 500.000 people in 116 cities in USA indicates that after eliminating different confounding factors, fine particulate (PM<sub>2.5</sub>) air pollution exposures were associated with significant increases in lung cancer mortality and each 10 ug /m<sup>3</sup> elevation in fine particulate air pollution was associated with 8% in cancer mortality

---

\*Corresponding author





**Table 1. Some genetic polymorphisms related to lung cancer.**

Gene	Polymorphism	Codon (SNP)	Protein Function
<b>CYP1A1</b>	Msp1 (CYP1A1*2A)	T6235C	Phase I: PAHs Activation
<b>CYP1A2</b>	CYP1A2*F	C734A	Phase I: HAPs, Nitrosamines and arylamines metabolism
<b>CYP2E1</b>	DraI  PstI	T7668A  C1091T	Phase I: Procarcinogens Activation (4- methylnitrosamine, aromatic amines
<b>CYP3A4</b>	CYP3A4*3	Met445Treo	Phase I: Drug metabolism. Procarcinogens Activation (PAHs)
<b>mEH (Epoxide hydrolase)</b>	EPHX1*3	Tir113His	Phase I: Procarcinogens Activation (HAPs)
<b>GSTs (Glutathion transferases)</b>	GSTM1  GSTT1  GSTP1	mu  teta deletion  pi deletion, Ile105Val	Phase II: Glutathion conjugation of hydrophobic and electrophilic compounds
<b>UGTs (UDP- glucuronosyltransferases)</b>	UGT1A1*28	Insertion/deletion of a repetead sequence TA, in the promotor region	Phase II: Glucuronic acid Conjugation of hydrophobic and electrophilic compounds
<b>NATs (N-acetyltransferases)</b>	NAT1*10	T1088A and C1095A	Phase II: Acetylation of aromatic amines and heterocyclic amines activation
<b>ERCC2</b>	XPD (NER)	Lis751Gln Asp312Asn	DNA repair
<b>XRCC1</b>	BER	Arg280Gln	DNA repair
<b>p53</b>	Codon 72	Arg72Pro	Cellular cycle regulation Tumor supressor
<b>MDR</b>	MDR1	C3435T	Drug Resistance



**Gil, L. and Adonis, M.**

particulate matter in Santiago, Chile. *Inhalation Toxicology*, 2000, vol. 12, no. 12, p. 1173-1183.

ADONIS, M.; MARTÍNEZ, V.; RIQUELME, R.; ANCIC, P.; GONZÁLEZ, G.; TAPIA, R.; CASTRO, M.; LUCAS, D.; BERTHOU, F. and GIL, L. Susceptibility and exposure biomarkers in people exposed to PAH-diesel exhaust. *Toxicology Letters*, 2003. vol. 144, no. 1, p. 3-15.

GIL, L.; KING, L. and ADONIS, M. Trends of polycyclic aromatic hydrocarbons levels and mutagenicity in Santiago's inhalable airborne particles in the period 1992–1996. *Inhalation Toxicology*, 2000, vol. 12, no. 12, p. 1185-1204.

IRARRÁZABAL, C.; ROJAS, C.; ARACENA, R.; MÁRQUEZ, C. and GIL, L. Chilean pilot study on the risk of lung cancer associated with a codon 72 polymorphism in the gene of protein p53. *Toxicology Letters*, 2003, vol. 144, no. 1, p. 69-76.

QUIÑONES, L.; LUCAS, D.; GODOY, J.; CÁCERES, C.; BERTHOU, B.; VARELA, N.; LEE, K.; ACEVEDO, L.; MARTÍNEZ, L.; AGUILERA, A. M. and GIL, L. CYP1A1, CYP2E1 and GSTM1 genetic polymorphisms. The effect of single and combined genotypes on lung cancer susceptibility in Chilean people. *Cancer Letters*, 2001, vol. 174, no. 1, p. 35-44.

POPE, C.A.; BURNETT, R.T.; THUN, M.J.; CALLE, E.E.; KREWSKI, D.; ITO, K. and THURSTON, G.D. Lung cancer, cardiopulmonary mortality and long-term exposure to particulate air pollution. *JAMA*, 2002, vol. 287, no. 9, p. 1132-1141.

Note: Electronic Journal of Biotechnology is not responsible if on-line references cited on manuscripts are not available any more after the date of publication.