Introduction To Biology Term Paper

Lung Cancer

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Contents

1 Abstract

Lung cancer is known to cause the most number of fatalities around the globe. We will try to look at some factors that cause lung cancer and some ways in which technology is involved in detecting it.

2 Understanding Cancer

Two very important genes that play a major role in understanding cancer are *proto-oncogenes* and *anti-oncogenes* - tumor suppressor genes. Our body has certain pathways and regulatory mechanisms. Mutations can cause an imbalance and chaos to these mechanisms. These mutations can occur due to environmental factors such as carcinogens or could be inherited. If any of these mutations cause the cell to divide longer than usual or not die easily then the cell is said to have lost control over cell division. This cell will then divide to form several such defective cells and those will further divide, producing mass numbers of defective cells - known as cancer.

2.1 Cell cycle

The cell cycle consists of the following phases: G1 - growth, S - DNA synthesis, G2 - growth and preparation for mitosis, M - mitosis which is cell division and G0 - rest. An adult cell doesn't spend a lot of its time dividing. The cell maintains a couple of regulatory measures to ensure that the cycle is followed smoothly and correctly. The transition from G1 to S phase is regulated by genes called *proto-oncogenes* that produce the necessary proteins. The genes that produce proteins that have a counter effect are known as *anti-oncogenes* (a.k.a tumor suppressor genes).

2.2 Apoptosis

Apoptosis is popularly known as *programmed cell death*. As a cell ages, it takes on more stress and can get damaged or naturally worn out. These cells must be removed. Apoptosis is a complex mechanism and mutations due to carcinogens can lead to altering its pathways. As a consequence the body fails to eliminate some cells and this causes a problem if they are pre-malignant neoplastic cells (these are abnormal growths that can grow into cancer). Defects in apoptosis can also lead to resistance to chemotherapy, radiation, and immune-mediated cell destruction.

3 Lung Cancer

Estimated New Cases*

Males			Females		
Prostate	240,890	29%	Breast	230,480	30%
Lung & bronchus	115,060	14%	Lung & bronchus	106,070	14%
Colon & rectum	71,850	9%	Colon & rectum	69,360	9%
Uninary bladder	52,020	6%	Uterine corpus	46,470	6%
Melanoma of the skin	40,010	5%	Thyroid	36,550	5%
Kidney & renal pelvis	37,120	5%	Non-Hodgkin lymphoma	30,300	4%
Non-Hodgkin lymphoma	36,060	4%	Melanoma of the skin	30,220	4%
Oral cavity & pharynx	27,710	3%	Kidney & renal pelvis	23,800	3%
Leukemia	25,320	3%	Ovary	21,990	3%
Pancreas	22,050	3%	Pancreas	21,980	3%
All Sites	**822,300**	**100%**	**All Sites**	**774,370**	**100%**

Estimated Deaths

Males			Females		
Lung & bronchus	85,600	28%	Lung & bronchus	71,340	26%
Prostate	33,720	11%	Breast	39,520	15%
Colon & rectum	25,250	8%	Colon & rectum	24,130	9%
Pancreas	19,360	6%	Pancreas	18,300	7%
Live & intrahepatic bile duct	13,260	4%	Ovary	15,460	6%
Leukemia	13,740	4%	Non-Hodgkin lymphoma	9,570	4%
Esophagus	11,910	4%	Leukemia	9,040	3%
Uninary bladder	10,670	4%	Uterine Corpus	8,120	3%
Non-Hodgkin lymphoma	9,750	3%	Live & intrahepatic bile duct	6,330	2%
Kidney & renal pelvis	8,270	3%	Brain & other nervous system	5,670	2%
All Sites	**300,430**	**100%**	All Sites	**271,520**	**100%**

These are some statistics on various types of cancer based in 2011. Lung cancer has the greatest numbers when it comes to fatality.

3.1 Smokers

About 75% of the global cases of lung cancer are attributed to smokers. We will be talking about tobacco based cigarettes. This seems to be the one of the major reasons as cigarettes are packed with harmful carcinogens. Cigarettes mostly consist of nicotine and tar - one of the major contributors to lung cancer. Some of the carcinogens a smoker can come across are polycyclic aromatic hydro- carbons (PAHs), aromatic amines, N-nitrosamines, benzene, vinyl chloride, arsenic, chromium and radon. Among these, PAHs and N-nitrosamines require metabolic activation to become carcinogenic, radon being radioactive can decay into bismuth and polonium.

There are a number of factors that can influence the chance of getting lung cancer. The composition - amount of nicotine and tar, presence and strength of a filter, number of puffs per minute and intensity of each puff - how deep one breathes in the smoke, are a couple of them. Deeper inhalation causes the smoke to reach the peripheral bronchi which lack the protective epithelial layer. It is observed that it increases the chances of adenocarcinoma.

3.2 Non-Smokers

About 25% of the global cases of lung cancer are attributed to non-smokers. They are ones who have smokes less that 100 cigarettes in their lifetime. Some factors that influence non-smokers getting lung cancer are: secondhand smoke - which is the smoke let out by smokers (still contains some carcinogens), environmental factors, exposure to solvents, paints, thinners, smoke, soot, or exhaust, radioactive material - radon, heavy metals - arsenic, asbestos, pollution (mostly air pollution) and genetic factors.

3.3 Genetic Factors

This is a multi-variable logistic model that considers factors such as smoking history, exposure to environmental tobacco smoke, occupational exposures to dusts and to asbestos, and family history of cancer.

Risk Factor	*P* Value	OR (95% CI)
Never smoker		
ETS (yes vs no)	.0042	1.80 (1.20–2.89)
Family history (≥2 vs <2)[a]	<.001	2.00 (1.39–2.90)
Former smoker		
Emphysema (yes vs no)	<.001	2.65 (1.95–3.60)
Dust exposure (yes vs no)	<.001	1.59 (1.29–1.97)
Family History (≥2 vs <2)[a]	<.001	1.59 (1.28–1.98)
Age stopped smoking		
<42 years	Reference	
42–54 years	.1110	1.24 (0.95–1.61)
≥54 years	.0018 (*P* for trend = .017)	1.50 (1.16–1.94)
Current smoker		
Emphysema (yes)	<.001	2.13 (1.58–2.88)
Pack-years		
<28	Reference	
28–41.9	.1932	1.25 (0.89–1.74)
42–57.4	.0241	1.45 (1.05–2.01)
≥57.5	<.001 (*P* for trend <.001)	1.85 (1.35–2.53)
Dust exposure (yes vs no)	.0075	1.36 (1.09–1.70)
Asbestos exposure (yes vs no)	.0127	1.51 (1.09–2.08)
Family history[b]		
0	Reference	
≥1	.0021	1.47 (1.15–1.88)

Ever since many models were build that. Some focused on family history of early onset lung cancer under the age of 60 years, susceptible genetic factors such as genetic markers to lung carcinogens, high-penetrance low-frequency genes and low-penetrance high-frequency genes.

A study has shown that lung cancer is twice as likely in case of family history of lung cancer and an increased risk for non-smoker. More specifically, they have linked it to the following region on the chromosome 6q23–25 (146cM–164cM). If we combine the two, smokers with family history of lung cancer, studies show that they are thrice as likely to get lung cancer.

Other studies include targeting the genes that are involved in absorp-

tion, metabolism, and accumulation of carcinogens in the lung tissues. With respect to metabolism, several enzymes are studied among which CYP1A1 is one of them. While there wasn't substantial data to link it to the occurrence of lung cancer, it was found to increase the likely hood of causing squamous cell carcinoma (type of skin cancer) by 55% in whites.

GSTM1 is a part of the GST gene. This gene in its null form is known to occur in half the population. An initial study indicated that there is a 17% increase in chance among the people who are GSTM1 null to have lung cancer. A later study conducted on a larger scale showed a 18% increase in chance among the people who are GSTM1 null to have lung cancer, thus strengthening the relation between the gene and lung cancer.

In order to identify some low-penetrance alleles that can influence lung cancer, a study performed a GWAS (genome-wide association study) scan of tagged single nucleotide polymorphisms in histologically confirmed non-small cell lung cancer (NSCLC). They identified these to be a region of the nicotinic acetylcholine receptor genes.

Studies on gene-gene interactions such the the ones that code for NAT2 and mEH with certain activity level have shown to increase the likely hood of lung cancer. Factors for variation in activity depends on whether or not the person smoke, exposure and susceptibility to carcinogens.

Several studies done on polymorphism in genes involved in DNA repair enzymes indicate a relation to lung cancer. It has been obsererved that chronic inflammation in lungs due to exposure to tobacco might be a factor leading to lung cancer. The genes that code for the enzymes (cyclooxygenase, metalloproteases) involved in repair of inflammation have been linked with an increase in likely hood of getting lung cancer.

Processes such as DNA methylation, histone deacetylation and phosphorylation can alter the way a gene expresses itself. It is observed that acquired or epigenetic changes to DNA chromosomes could potentially lead to lung cancer.

Mutagen sensitivity has been observed to influence the chance of getting lung cancer. It is observed that smokers with mutagen sensitivity were more likely to get cancer compared being either a smoker or having mutagen sensitivity.

3.4 Other factors

There are several other factors such as age, gender, race and ethnicity, other lung complications, infections, second hand smoking, biomass and wood-smoke exposure, environmental air pollution, occupational carcinogens such as arsenic, asbestos, beryllium, chloromethyl ethers, chromium, nickel, radon, siicon, etc., and several others.

4 Prevention

As we have seen above, we could try and avoid environmental tobacco smoke, exposure to asbestos and radon, air pollution by wearing a mask, etc. We could also maintain a healthy diet. One of the major reason is smoking and avoiding which drastically reduces the likely hood of getting lung cancer. Studies show that people who quit smoking for more than 15 years have about 80% - 90% reduction in their risk for lung cancer compared to those who continue to smoke. Regular health checkups could lead to early detection of cancer and reduce the chances of fatality. Chemoprevetion is another way lung cancer could be prevented in the early stages. It is basically the method of using specific substances (natural or non-natural agents, dietary or pharmacologic) that interfere with the development of cancer cells by preventing the DNA damage or by halting the progression of premalignant cells. Two of these substances are β-carotene and isotretinoin which have been obsevred to increase the risk of lung cancer in case of smokers. Some other substaces include COX inhibitors, prostacyclin analogues, leukotriene modifiers, green tea, and broccoli sprout extracts. Although these have not been proved to be very effective. The most effective way for

prevention of cancer still remains avoiding or ceasing to smoke.

5 Some Technological Advancements

1. The DeepCC model focuses on molecular subtyping of cancer. It is a novel supervised cancer classification framework that classifies the cancer subtypes using deep convolutional neural networks. Its implementation is based on MXNet and can run on both CPU and GPU. It has been shown to have higher accuracy, specificity and sensitivity compared to other classification models such as random forests, support vector machine, gradient boosting machine, and multinomial logistic regression. It took up colorectal cancer and breast cancer for its case studies.

2. Rajesh P, Murugan A, Murugamantham B and Ganesh Kumar S came up with a monile app that spreads awareness and enables health tracking. The added benefit of convenience is a big plus point. They use CT scans (computed tomography) as training data for their artificial intelligence model. The DICOM (Digital Imaging and Communications in Medicine) image data along with all the information extracted from the training model is stored in a numpy file.

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