You need a stronger understanding of the topic. Do a pubmed search for : "miRNA regulation melanoma 2013" Then click Review (article types left hand side). Repeat for 2014 or other years as needed. Print one or two, read them and understand them.

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You need to tell this story in a way that the progression makes sense. This means that the order of topics is very important. For instance, it was very confusing that you mentioned microRNAs and then switched to genomic markers (by which you meant genes identified by mutation.) You followed this with histone modifications. This is odd because microRNAs are one of your examples of epigenetic regulation, mutated genes are not, and histone modifications are epigenetic. So you flanked a genetic change with two epigenetic changes – why? Sometimes that means that you need to tell us why you are saying something. An example would be why you described genetic changes (mutations).

Wikipedia Article on Epigenet

Introduction

How and/or why does melanoma occur in people? Melanoma is a rare but aggressive malignant cancer that originates from melanocytes. These melanocytes are cells found in the basal layer of the epidermis that produce melanin under the control of melanocyte-stimulating hormone. Although the disease is atypical in all skin cancers, it is surprisingly held responsible for more than 50% of skin cancer-related deaths in young adults (Sigalotti *et al,* 2010). The high metastatic qualities and death rate, and also its prevalence among people of younger ages make melanoma a highly researched malignant cancer. As the case might be for other many cancer diseases, epigenetics modification is suspected to hold clue for this daunting disease.

In other places you use the numbered reference format. You need to do so here.

As written means that Epigenetics do not "affect" DNA changes. But what you really mean is that the heritable changes are not the products of changes in DNA sequence. Please figure out a rewrite.

Epigenetics is the term used to refer to heritable changes in gene expression that does not affect changes to DNA sequence. These changes occur regularly in nature but can be influenced by factors such as the environment, ~~ones~~ life style, age and state of disease. its modifications can be the manner in which cells differentiate to become different cell types such as skin, liver and brain cells. The changes can also have damaging effects, which can result in fatal diseases such as cancer.

Does not make sense.

What changes?

Roles microRNA play in melanoma development

Give a short definition of what a microRNA is.

For long now, scientists have wondered how melanoma cells travel from major tumors found on the surface of the skin to the liver, brain, lungs and other organs where they become very destructive, resistant to treatments and even cause death. They wonder why and how these cells become defective and eventually cause harm to people, and they are convinced that it all can be linked to a short strand of RNA called microRNA.

Not all miRNAs have been linked to cancer. Why do you state this?

To what does "it" refer? – all miRNAs? If so, then this statement is probably not true. Why can't under expression of miRNAs cause cancer like phenotypes. Be more specific.

encoded

"Daunting" iis an unusual word that you have already

MicroRNA serves in blocking the expression of proteins ~~encrypted~~ by messenger RNAs; they have been linked, recently, to the over or under expression of several genes associated with cancer and other daunting diseases such as heart diseases. It becomes harmful when it is overly-expressed in metastatic melanoma tissues and cell lines (NYU Langone Medical Center). And this elevated expression is what turns it into an oncogene, a gene that is involved in tumor formation and progression. MicroRNA 182, which contains some oncogenes like BRAF and C-MET, belongs to a group that is found in a genomic region, specifically on chromosome 7. this microRNA is known to be amplified regularly in melanoma.

The miRNA "contains" BRAF and C-MET? This makes no sense.

TABLE 1. *Genes altered by mutation, deletion, or amplification in malignant melanoma*

Gene type	Gene	Most frequent type of alteration	Frequency (%)
Proto- oncogenes	*NRAS*	Mutation	15- 25
	BRAF	Mutation	50- 70
	KIT	Mutation	2- 10
	CDK4	Mutation, amplification	0- 9
	CTNNB1	Mutation	2- 23
	MITF	Amplification	10- 16
	CCND1	Amplification	6- 44
	PIK3CA	Mutation	<5
	AKT3	Amplification	40- 60
Tumor Suppressor Genes	*INK4A*	Mutation, deletion	40- 87
	ARF	Mutation, deletion	40- 70
	PTEN	Mutation, deletion	5- 40
	TP53	Mutation	0- 25

Because this is an article on Epigenetics you have to introduce other topics (mutations that promote melanoma) carefully to avoid confusing people. Usually, you would do this something like this: "Many cancer-causing genes were originally identified mutations that alter the activity of the gene or protein and produce cancer." You could say it differently, but embedded into it should be an indicator that this sentence and this table are not about epigenetics.

Genomic markers

Actually, your reader will not see this. It is just a list of genes with no pathways identified.

Many cancers are caused by mutations in genes involved in maintaining genomic integrity or in regulating cell growth. In Table 1, it can be seen how many genomic pathways are mutated and their frequency of occurrence. Many pathways have been extensively researched and their mechanisms and roles in cancers have been well documented, as seen in Table 1. These mutations affect different biological pathways within the cell, and attribute to the complexity of combating melanoma. No one single mutation can cause melanoma, but it can be asserted that some mutations are more deadly than others, as shown in table one and the frequency of occurrence of different gene alterations. Extensive research has been done on cancer cells and their biological pathways, specifically in melanoma, because of their prevalence and deadliness. Below is discusses different genes from different pathways that ~~appear in melanoma in various ways~~ are thought to contribute to the appearance of melanoma.

The table does not show any of this documentation.

"different genes" "different pathways" "various ways" <-- This is too many general modifiers.

BRAF

BRAF is one of the many genes that can mutated in melanoma. It is in the second part of the Ras-Raf-MEK-ERK pathway (also known as the MAPK/ ERK pathway) which deals with cell signalling, cell division, and can trigger transcription of various genes. Mutations in the Ras-Raf-MEK-ERK pathway are very common in cancers, and BRAF mutations are found in 50- 70% of melanomas. A mutation in the RAF pathway can cause a cell to keep dividing, leading to fast growing cancers. BRAF mutations can almost always be attributed to the V600E mutation. V600E is a mutation in the amino acid chain where the 600 position valene is mutated. The V600E mutation is found in 90% of BRAF mutations, because it causes the activation of the BRAF gene[3]. If the overactive BRAF gene is knocked out, the cell will die, making BRAF an excellent target for therapeutics[4].

NRAS

NRAS was one of the first genes found mutated in melanoma. It is part of the Ras family, which is prevalent in many cancers and also in the first part of the Ras-Raf-MEK-ERK pathway. Ras is a proto- oncogene and involved in cell signaling. When switched on, it causes many biological processes like cell growth and differentiation to become active, which are key in the creation of cancer cells. If the Ras portion of the Ras-Raf-MEK-ERK pathway is damaged or mutated (like in most cancers), it can be extremely difficult for

the signal cascade to recover and perform the correct action. The removal of NRAS kills cells[5], and it has also been traced to maintaining the growth of melanoma cells[2]. NRAS is found it 15- 25% of melanoma cells[6].

AKT3

AKT3 is a locus on the AKT gene. It is primarily found to deal with cell proliferation, differentiation, and apoptosis among many other important cell life processes, and it is the least known about of the AKT loci. The AKT gene mainly functions as a insulin regulator, but can also inhibit apoptosis of cells and prolong their life. Increased activity from AKT can cause cells to grow and spread, and much of the increased expression comes from the AKT3 locus; with the removal of this locus, the cell dies[7]. This locus is found in 40- 60% of melanomas[7].

TABLE 2. *Genes targeted by promoter hypermethylation in malignant melanoma*

Gene	Frequency (%)
RASSF1A	36- 57
APC	
PYCARD	
RARB	
MGMT	0- 34
DAPK	19
3- OST- 2	56
CDKN1B	0- 9
INK4A	10- 20
HOXB13	20- 33
SYK	30- 89
PRDX2	8

First, you focus on mutations that can contribute to melanoma, then you switch gears and start talking about epigenetic changes. I thought that you were identifying genes by mutation so that you could talk at length about how they are regulated by epigenetics. But the examples that you discuss in the mutation section are not in this epigenetics table. It is OK to say that genes have been identified by mutation. But you are being confusing about it.

PTEN	0- 62

Histone Markers

Is table 2 showing us CpG methylation changes or histone methylation changes? I really think that you are confusing the two.

The chemical modification of histones can have epigenetic consequences leading to persistent changes in gene expression. Certain histone modifications have been linked to melanoma, as seen in Table 2. The hypermethylation of genes can cause cancers to form or can cause important regulatory sequences to become inactivated. Most genes that are hypermethylated are not mutated or suffer from deletions, like the genes in Table 1[2], although some overlap can be seen from the tumor repressor genes in Table 1.

INK4A

INK4A is a tumor repressor gene found in 10- 20% of histone marker modifications and 40- 87% of gene alterations in melanoma cases[8]. The hypermethylation of this gene can cause it to become inactivated[9]. When INK4 is inactivated, it causes an interuption of CDK4 and CDK6 which normally stop cell growth in the G1 phase of cell division. When this happens, there is no regulation in the cell and it grows quickly and becomes cancerous.

SYK

SYK is a gene that, when hypermethylated, loses function[11]. This gene is found in 30- 89% of melanoma cases[2], and causes cells to grow quickly. This metabolism quality is important in the metastasis of the cancer cells, and when hypermethylated, the growth and spread of cells slows considerably[12]. This is a controversial finding with inconclusive results, though. Some findings show that SYK aids in tumor repression, while others find that it is a transforming factor that facilitates cancer formation.

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