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The Cell Cycle and its Regulation

When cell division occurs, each new cell has a copy of all the genetic material, and these daughter cells are completely identical, so how does this work?

How do we get two cells from one?

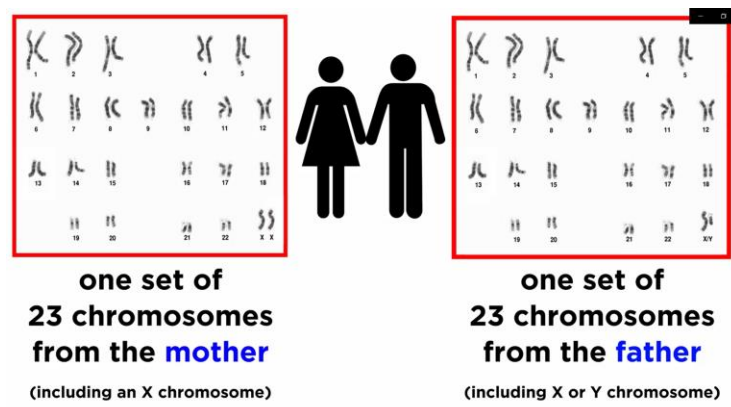
The first thing we have to do is understand how all the DNA is arranged in a cell.

Each daughter cell needs a complete copy of all the genetic information, or genome, and while prokaryotes often have just one circular DNA molecule, eukaryotic cells have many different linear DNA molecules, called chromosomes.

All of this material has to undergo replication, and then the two sets must be separated before the cell divides, leaving each daughter cell with a copy.

Different eukaryotic species have different numbers of chromosomes, and us humans have 46 chromosomes in all our somatic cells, which are basically all your cells, excluding the reproductive ones.

That's a set of 23 chromosomes from each parent.



Each **chromosome** consists of a DNA molecule wrapped around proteins called histones to form nucleosomes.

This chromatin fiber undergoes supercoiling for storage when not in use, but will uncoil to undergo replication.



To understand exactly how DNA replication works on the molecular level, all the DNA in a chromosome is copied, resulting in two identical sister chromatids.

These are attached at the center by a centromere, with the chromosomal arms extending on either side.

Later, when the cell divides, the sister chromatids will separate and get pulled into each of the two daughter cells.

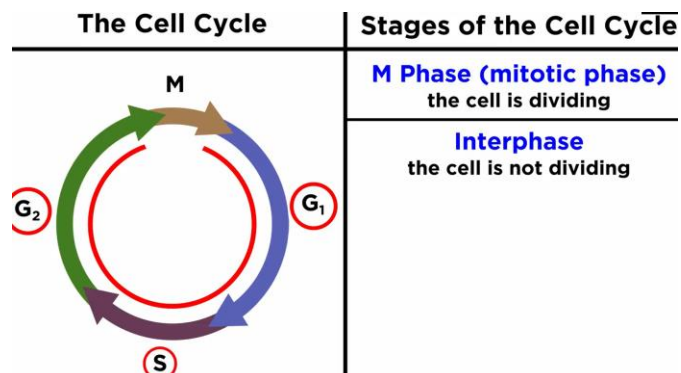
So when does the genome replicate, when does it get pulled apart, and when do we get two completely new cells?

Let's examine the different stages of the cell cycle now

Although cells do divide, most of the time they are not dividing.

They're just being cells.

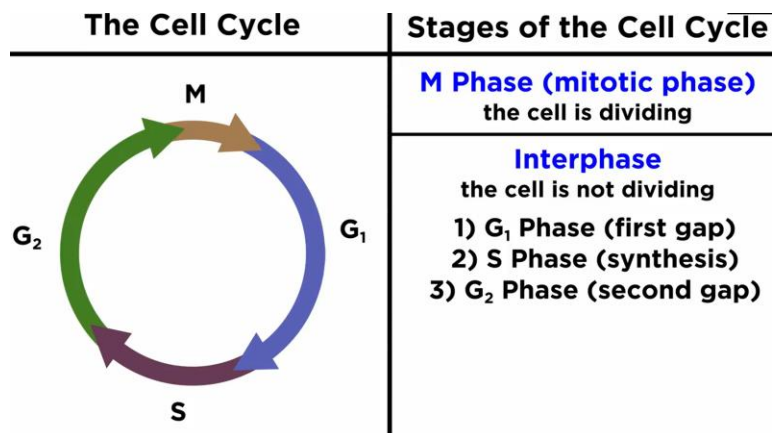
The time that a cell spends dividing is called the M phase, or mitotic phase, and the time spent not dividing is called the interphase, or the phase in between divisions.



The interphase is comprised of three subphases.

Those are the G1 phase, or first gap, the S phase, or synthesis, when the genome gets copied, and the G2 phase, or second gap.

These gap phases were named as such because it first appeared that not much was happening during these times.



Later we came to understand that there is an incredible amount of cellular activity that must occur in order to prepare for the S phase and the M phase.

This is because the new cells don't just need their own genome, they also need all of the other cellular components and organelles, so these must be produced as well.

The G1 phase, which marks the beginning of a cell's life, involves cell growth.

Some cells divide very infrequently, or not at all, so cells can spend a long time in this phase, or a related phase called G Zero.

Other cells that divide more rapidly may spend only a few hours in this phase.

In adult humans, the S phase takes ten to twelve hours, results in two identical copies of the genome.

The G2 phase takes about four to six hours, and involves more growth and preparation for cell division.

And then the M phase, or mitosis, has the cell dividing into two daughter cells, which takes about an hour.

Other animals have significantly different rates for these phases, as do human embryonic cells.

What controls the cell cycle?

How does a cell know when to enter the next phase?

This is crucial to understand, because some cells inside the human body, like skin cells, are dividing very frequently, while liver cells don't divide much at all, and fully formed nerve cells never do.

These discrepancies can be accounted for when we examine the ways that the cell cycle is regulated on the molecular level.

This is called the cell cycle control system, and it is regulated by small signaling molecules in the cytoplasm.

These trigger and coordinate key events throughout the cycle.

The Checkpoints

There are moments during or in between phases that are called checkpoints, where the cell must receive a specific signal to move forward.

The First Checkpoint

One of these occurs during the S phase, to ensure that DNA replication occurs without any problems.

The Others Checkpoints happen during the G₁ phase, at the end of the G₂ phase, and during the M phase.

The Second Checkpoint (The restriction point)

There is also a checkpoint during the G₁ phase that is called the restriction point.

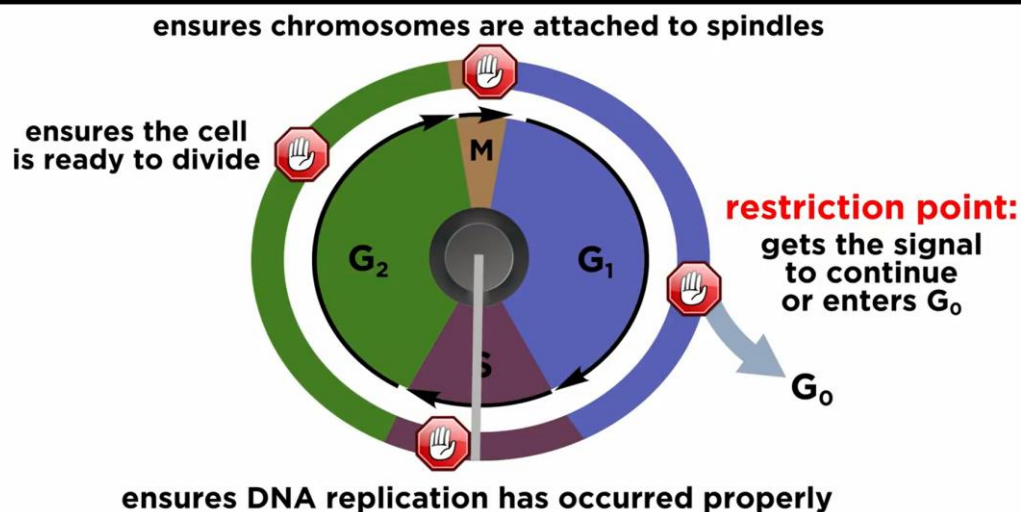
This is a stop point that must be overridden by a signal in order to continue to the rest of the cycle.

In absence of this signal, the cell remains in the G₁ phase or moves into the G Zero phase, which is a nondividing state.

Most of our cells are in the G Zero phase at any given time, but these can be called back into the cell cycle by external signals like growth factors, which can be released during injury to stimulate cell growth to heal the wound.

So we can think of the G₁ checkpoint as the primary point where the cell determines whether it will divide or not.

The Cell Cycle Control System



The Third checkpoint

The third checkpoint is in the M phase, and it governs the separation of sister chromatids during mitosis, which we will learn about later.

If cells are dividing they also need to know when to stop, like the way cells in a culture will stop dividing once they have filled up their container.

This is called **density-dependent inhibition**.

If the cells were to divide further, there would be no room, and they would all suffer.

Alternately, if some are removed, they continue dividing again to fill up the vacancy.

This occurs due to surface proteins on each cell.



If they bind to receptors on adjacent cells, this sends a signal that inhibits cell division, even in the presence of growth factors, so only the ones with empty space nearby continue to divide.

So what happens when regulation of the cell cycle goes wrong?

In a word, **cancer**.

Cancer involves cells that are dividing out of control, which leads to the development of a tumor.

Cancer cells are like regular cells, except that they do not follow the instructions carried by the signals that normally regulate the cell cycle.

They may continue to divide even when no growth factor is present, or when there is no room for more cells.

This can happen for many different reasons, which is why there are so many kinds of cancer, and they all stem from a genetic abnormality of one kind or another.

A genetic mutation will alter the product of gene expression, and if this resulting protein is crucial for regulating the cell cycle, it can lead to what we call “transformation”, or behaving like a cancer cell.

Sometimes if there are strange new proteins on the surface, this abnormal cell can be recognized by the immune system and destroyed, but if not, it can divide rapidly and produce a tumor.

This is why cancer treatment relies so heavily on understanding the science behind cell division and cell cycle regulation, as any cancer treatment that hopes to be even remotely effective absolutely must address the issue on this fundamental biological level.

Let's learn more about cell division now.

Wishing you the best of luck
Dr. Maissoun Ziadeh

The Cell Cycle	دورة الخلية	Different Rates	معدلات مختلفة
Regulation	تنظيم	Embryonic Cells	الخلايا الجنينية
Division	انقسام	Controls	يتحكم
Occurs	يحدث	Frequently	متكرر
Identical	متطابق	Fully Formed	الكاملة التكوين
Arranged	يترتب	Nerve Cells	الخلايا العصبية
Linear	خطي - مستقيم	Discrepancies	التناقضات
Undergo	تخضع	Accounted	حساب
Replication	تضاعف	Signaling Molecules	جزيئات إشارات
Somatic	الجسدية	Trigger	تأثير
Excluding	باستثناء	Coordinate	تنسيق
Reproductive	التكاثرية	Checkpoints	نقاط التفتيش
Wrapped	ملفوف	Receive	تتلقى
Nucleosomes	الجسيمات النووية	Ensure	لضمان
Supercoiling	الالتفاف الفائق	Categories	فئات
Uncoil	تفكك	Activate	تنشط
Attached	تلتصق	Deactivate	تعطل
Pulled	تُسحب	Phosphorylation	الفسفرة
Examine	نفحص	Briefly	بإيجاز
Stages	المراحل	Receptors	المستقبلات
Mitotic Phase	الطور الانقسامي	Signal transduction	نقل الإشارة
Interphase	الطور البيني	Kinases	إنزيم ينقل مجموعات الفوسفات
Comprised	يتكون	Cyclins	عائلة بروتينية
First Gap	الفجوة الأولى	Maturation-promoting	تعزيز النضج
Synthesis		Degraded	يتدهور
Second Gap	الفجوة الثانية	Restriction	التقييد
Involves	تتضمن	Overridden	تجاوز
Infrequently	نادر	Absence	غياب
Related	مرتبط	Called Back	تستدعي
Rapidly	بسرعة	Injury	الإصابة
Preparation	التحضير	Governs	تحكم
Mitosis	الانقسام الفتيلي	Separation	فصل

Culture	مزرعة- بيئة	tumor	الورم
Container	الحاوية	instructions	التعليمات
Density-dependent	المعتمد على الكثافة	reasons	أسباب
Inhibition	التثبيط	stem from	تتبع من
further	أكثر	abnormality	خلل
no room	لا مكان	mutation	الطفرة
suffer	يعاني	alter	تغير
Alternately	بالتناوب	expression	التعبير
to fill up	لملء	transformation	التحول
vacancy	الشاعر	abnormal cell	الخلية غير الطبيعية
surface proteins	البروتينات السطحية	recognized	يتعرف
adjacent cells	الخلايا المجاورة	immune system	للجهاز المناعي
cancer	السرطان	destroyed	تُدْمَر
involves	يشمل	relies	يعتمد
leads	يؤدي	remotely effective	فعال عن بُعد
development	تطور	fundamental	الأساسي

