Retinoblastoma

(hopefully keeping your eye)

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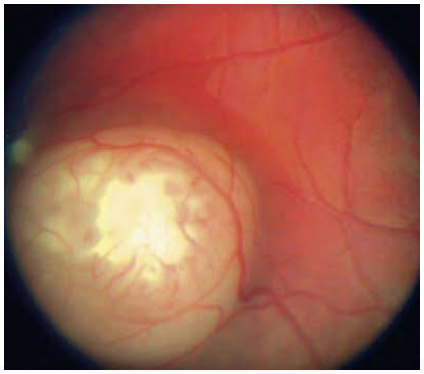
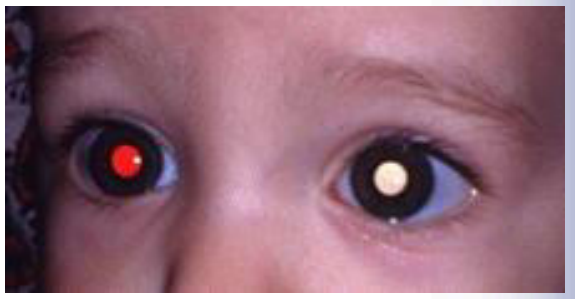
Physiology

- Retinoblastoma is rare eye cancer that specifically develops in the retina.
- The disease is early onset, typically affecting the child before the age of 5.
- Retinoblastoma is an autosomal dominant disease with a rate of 1 in 15,000 children.
- Nearly 60% of all cases are nonhereditary.

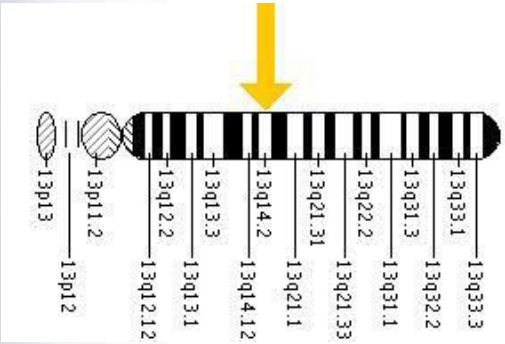
Symptoms

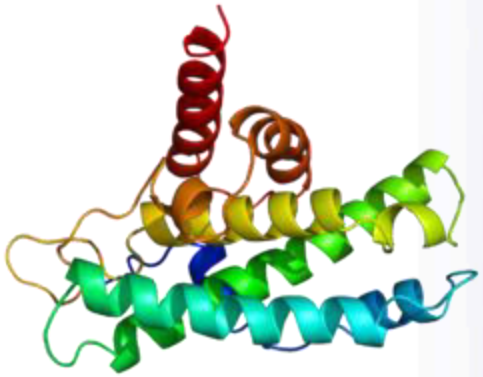
- Leukocoria, also known as "cat's eye reflex", which is a visible white spec in the eye visible if a tumor has developed.
- Other symptoms include redness, irritation, and pain around the affected eye(s).
- Left untreated, the cancer can cause permanent damage to the eye, such as strabismus, a condition where the eyes are not aligned with each other or even blindness.





Molecular Cause

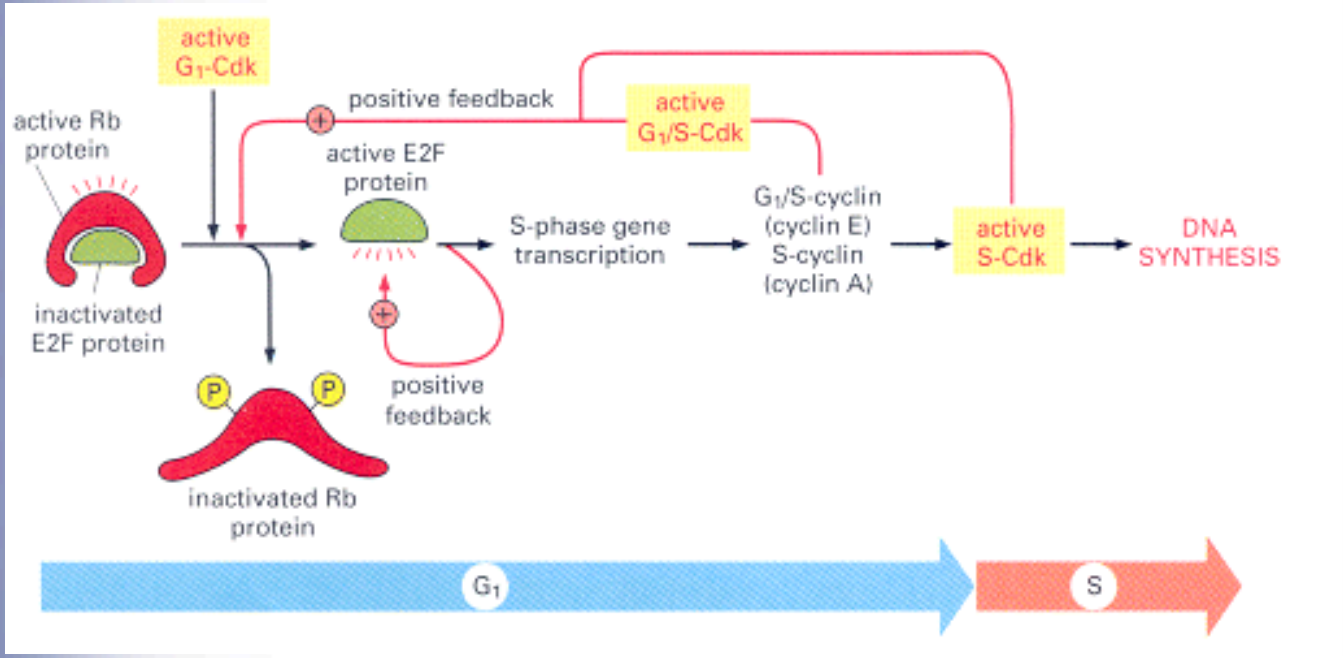




- The retinoblastoma gene creates retinoblastoma protein (pRb), a tumor suppressing protein.
- The Rb gene is located on the lower arm of chromosome 13.
- In the hereditary form of retinoblastoma, cells of the body lack a copy of the normal Rb gene. In order to develop the tumor, the remaining normal copy of the gene is lost/inactivated due to a somatic mutation.
- In nonhereditary retinoblastoma, again, both copies of the Rb gene must be defective for the disease to arise. This means that two somatic mutations must occur.
- Even though it takes two copies of the defective gene to show symptoms of the disease, a person who has one copy of the defective gene will almost always have the second copy of the gene mutate.

Molecular Cause (cont.)

- There are 370 documented mutations of the Rb gene, most of these mutations cause retinoblastoma. These mutations causes a change in the shape of pRb, preventing it from binding to and deactivating a transcription factor of the E2F family.
- pRb binds to E2F, preventing it from starting the transcription of S-phase genes. When G1-Cdk gathers, pRb is phosphorylated and pRb unbinds with E2F.
- If pRb is created at all in the cell, it does not necessarily mean that the cell will rapidly divide since there are also other proteins that perform similar functions to pRb and can bind and inactivate E2F transcription factors.



Current Treatments

- Current treatments for retinoblastoma involve removing the tumor with surgery or other means.
- Chemotherapy is an option for people who have developed large tumors. Most of the time, drugs are injected though a vein, or taken orally, so that it can reach the bloodstream and travel throughout the body. Drugs can also be injected around the eye for more advanced stages of the tumor. The drugs help in shrinking the size of the tumor.
- The most common method of treating retinoblastoma today is through cryotherapy. This method treats small tumors and involves using a small probe that is placed next to the tumor, freezing a layer of the cells, which would be sliced off. The process of freezing and slicing is repeated as long as the tumor is visible. The process may be used along with chemotherapy.
- Enucleation is a option taken by those who have large tumors that have not yet spread to other parts of the body. Enucleation is when the eye and its optic nerve is removed. Surgery on other parts of the face near the eye is not needed during enucleation. This type of surgery is quick, taking no more than an hour. After enucleation, a child is given a prosthetic, glass eye, which is replaced every couple years until the child stops growing.
- If both eyes suffers from advanced stages of the tumor, one eye would be enucleated, while the other undergoes other types of treatments in order to preserve some sight.

Proposed Cure/Limits

- All the current treatments are applicable once a tumor has formed. I am proposing a method which involves the injection of pRb around the retina so retinal cells do not lack the pRb if a cell happen to have its second Rb gene spontaneously mutate.
- Firstly, Rb gene must be extracted and converted into a plasmid to be placed into a bacterial cell. The bacterial cell will produce pRb, which can be harvested. Rb genes do not vary at all between normal people, so we should expect the pRb produced by bacteria to not differ from pRb produced by human cells.
- Before pRb can be injected to the retina, a simple, quick surgery is done to cut a slit into the sclera, the outermost, protective layer of the eye. Under the sclera is the choroid and retina, which is where pRb can be injected.
- The pRb injected around the retina will diffuse into the cell, where it will hang out in the cytoplasm. If the cell requests that pRb is needed, nuclear transport factors that normally pick up pRb will take into the nucleus the pRb that had diffused into the cell.
- Once inside the nucleus, the pRb that had been injected should function normally.

Limitations

- There is no evidence of how long pRb can possibly last in a cell.
- We can not say for certain whether injected pRb may ever reach the cytoplasm or nucleus.
- It is unclear about how much pRb must be injected.

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Images

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