Longwave ultraviolet light induces the aging-associated progerin in melanocytes
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**BACKGROUND**

**Hutchinson Gilford Progeria Syndrome (HGPS):**
- genetic disorder resulting in the premature aging of many organs, including the skin
  - skin abnormalities:
    - light brown spots on the neck, scalp, thorax and limbs, predominantly at sun exposed areas
    - hypopigmented regions
    - indurated, inelastic and sclerodermatous skin
    - highly visible veins
    - loss of subcutaneous fat
    - skin is thin, dry and atrophic, with hyperkeratosis and decreased turgor
- caused by an autosomal dominant mutation in the LMNA gene, resulting in alternative splicing and production of a mutant lamin A protein, progerin
- isolated fibroblasts from HGPS patients feature:
  - misshapen nuclei
  - increased lobulation of the nuclear envelope
  - thickening of the nuclear lamina
- recent studies revealed that cells of healthy, elderly individuals acquire nuclear defects similar to those observed in cell acquired from HGPS patients, due to sporadic activation of the same cryptic splice site affected in HGPS
- suggests that the process of aging may be related to the production of progerin

**Aging:**
- Intrinsic aging: progressive degeneration, similar to that observed in internal organs
- Photoaging: a form of extrinsic aging that results from environmental exposure, especially ultraviolet radiation
- Photoaging may accelerate processes involved with intrinsic aging
- Unlike keratinocytes, which have a high turnover rate, melanocytes do not proliferate greatly, and thus may be more likely to accumulate progerin over time.
- Previous studies in our lab indicate that progerin accumulates in fibroblasts, a cell population which similarly has a low proliferation rate

**Overall Goal:** to determine if the skin hypopigmentation observed in photoaging due to melanocyte senescence is caused by UV-induced progerin accumulation

**METHODS**

- Expose neonatal and adult melanocytes to UVA and UVB radiation.
- Isolate mRNA at 8hr and 24 hr time points.
- Use q RT-PCR to determine levels of gene expression of progerin relative to unexposed sham.

**RESULTS**

**CONCLUSION**

These results provide preliminary evidence that progerin protein accumulation may play a role in photoaging of the human pigmented system.

**FUTURE PROJECTS**

**REFERENCES**

Hennekam RCM. Hutchinson-Gilford progeria syndrome. PNAS. 101: 8963-8968, 2004

**QUESTION**

Does UV radiation induce expression of progerin in human melanocytes?

UVA, but not UVB, induces progerin mRNA in neonatal and adult melanocytes in a dose-dependent manner.

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