Journal of Interdisciplinary Science Topics

Mystique: The Ultimate Mutant

Leah Ashley
The Centre for Interdisciplinary Science, University of Leicester
19/02/2016

Abstract
This paper puts the powers of the mutant Mystique, seen in the Marvel Universe, into a biological context by exploring the genes she uses to change her appearance. These genes may be pre-existing and required to mutate or completely novel. It was found that several aspects of her appearance would be able to change, but over a much longer timescale than depicted in the films and comics, and possibly at a detriment to her health.

Introduction
Mystique has been shown to exhibit powers that render her able to disguise herself as another human, regardless of age, gender or race, by psionically controlling the cells of her body. As well as being able to control changes in hair type and colour, eye colour, skin tone and body proportions, she is also able to camouflage herself by changing the pattern and texture of her skin [1].

This paper assumes that Mystique's powers are the results of possessing additional genes seen elsewhere in nature and the ability to change the expression of her genes. These assumptions are based on the observation that Mystique has blue skin and yellow eyes and so possesses genes that do not exist in normal humans. Additionally, her decreased aging and ability to heal quickly points towards mutations in DNA repair mechanisms and cell proliferation signalling pathways [1]. The paper assumes that Mystique cannot mutate her genome to change her gender (merely her appearance), based on her phenotype and ability to conceive.

Skin, hair and eyes
Melanin is a natural pigment that absorbs light and is produced by melanocyte cells. Melanin levels contribute to skin, hair and eye colour [2]. The gene loci responsible for melanosomes – the organelles which synthesise, store and transport melanin – are likely to have the most significant contribution to pigmentation. Different races show different melanosome structure, so Mystique must be altering aspects of cell signalling pathways that control how the melanosomes are packaged [3].

16 genes have been discovered to determine human eye colour; a number are also believed to contribute to skin and hair colour [4]. The most significant of these genes are OCA2 and HERC2. OCA2 strongly affects eye colour by acting as a determinant of brown or blue eye colour, and mutations in the gene result in ocular albinism [2]. MC1R, commonly known as the 'red hair gene', is believed to have a very strong effect on hair colour, however IRF4, SLC24A4, KITLG, POMC and HCL3 are also highly associated with hair colour [5, 6, 7].

Specific genes that determine skin colour and the occurrence of freckles have also been identified. In addition to those that contribute to hair colour (IRF4, SLC24A4 and MC1R), TYR and MATP (genes that also determine eye colour) have been linked to variation in skin pigmentation [3, 6].

MATP and TYR have been linked to controlling both eye and skin colour, MC1R to hair and skin colour, and IRF4 and SLC24A4 to all three [7]. These genes are likely to be the first that Mystique would alter to create the biggest difference with the fewest mutations, but hold different significance for the traits between geographical populations [8]. The genes of focus will depend on whom Mystique is impersonating. One single nucleotide polymorphism is able to contribute greatly to the phenotype, therefore Mystique could dramatically alter aspects of her pigmentation in the time it takes to regenerate cells [9]. This is decades for iris and skin melanocytes [10, 11] and 3-5 years for hair melanocytes [12]. These rates could be increased if Mystique were to mutate genes involved in cell proliferation and senescence.

Pattern

Mystique's ability to change the patterns on her skin as camouflage could be similar to the ability of various cephalopods (such as cuttlefish). These possess chromatophores similar to the melanocytes in humans, however the classes of pigments span a wider range of colours. Some classes also contain nanocrystals that reflect light to create a shine. The chromatophores of cuttlefish are surrounded by muscles that are able to change the cells between punctate and expanded states, based signals from motor centres of the brain based on visual cues [13][14]. This produces a quicker colour-change response than the pigment dispersal mechanism used by vertebrates like the chameleon [15].

The cuttlefish has 6 reflectin genes that relate to its development of iridosmes and effective camouflage [16]. These genes may be part of the additional genes Mystique possesses. The gene PAX7A controls chromatophore development in the Japanese rice fish, and SLC2A15B is important to chromatophore differentiation [17]. SLC2A15 is similar to human SLC2A9, and PAX7A could be related to the human PAX7 gene that regulates muscle tissue formation [17][18]. With considerable mutation in her genome, Mystique may therefore show similar surface properties as the Japanese rice fish.

Body proportions and age

Body proportions are affected significantly by both genetics and environmental factors. Weight cannot be lost or gained through genetic mutation and cell renewal. Mystique is able to alter her size but not her mass [1], therefore changes in weight are attributed to an unexplained superpower. Genes that Mystique might mutate in order to facilitate changes in weight are those related to obesity: POMC, PCKS1, PCKS2, NTRK2 and MC4R [19, 20].

One lower limit for the total number of loci influencing human height is 180 genes [21]. Mystique may be able to initiate a mutation causing overexpression of GPR101, causing the symptoms of gigantism and allowing her to increase her height [22]. Based on famous cases and assuming a consistent growth rate (Table 1), the over 100-year-old Mystique [1] may be able to grow at a rate of around 15cm per year (assuming that she grew at the rate of a child with gigantism).

Case	**Age (years)**	**Height (cm)**	**Growth rate (cm/year)**
Robert Wadlow	14	226.0	16.14
Anna Swan	15	210.0	14.00
André the Giant	12	190.5	15.88
Giant Gonzales	14	193.0	13.79
Mean			14.95

Table 1) Growth rates of people documented with gigantism [23, 24, 25, 26].

She may be able to accelerate her growth with further mutations increasing the excess of growth hormone. The health risks associated with mutating the body in order to induce shrinkage, such as osteoporosis and sarcopenia, are likely too great to be part of Mytique's regular shapeshifting, and so this power of reducing her size is attributed to another superpower.

Mystique's ability to appear older could result from mutations causing Progeroid syndromes. These mutations typically cause DNA repair defects or alter lamin A, which is important for the structure of the nucleus [27]. The symptoms of these syndromes such as photosensitivity, high risk of cancer and problems with internal organs, make it unlikely that such mutations would be efficient [28, 29].

Conclusion

Mystique is an embodiment of the power of genetic mutations. She may be able to achieve reflective skin and rapid body growth, and create imitations through changes in skin, hair and eye colour based on a low number of SNPs in specific genes. However, these changes would not at all be as instantaneous as they are shown in the films and comics, taking up to decades to achieve.

Many of the mutations discussed may lead to unwanted side effects, or be unachievable in a short timescale without further altering genes controlling cell proliferation and DNA repair. This level of mutations would increase the likelihood of cancer, so it is fortunate that Mystique has the power of super-healing.

References

[1] Marvel Database, (2016). Raven Darkholme (Earth-616). [online] Available at: http://marvel.wikia.com/wiki/Raven_Darkholme_(Earth-616) [Accessed 03/02/2016].

[2] Sturm, R. and Frudakis, T. (2004) *Eye colour: portals into pigmentation genes and ancestry*. Trends in Genetics, **20**, 8, 327-332.

[3] Sturm, R., Box, N. and Ramsay, M. (1998) *Human pigmentation genetics: the difference is only skin deep*. Bioessays, **20**, 9, 712-721.

[4] White, D. and Rabago-Smith, M. (2010) *Genotype–phenotype associations and human eye color*. Journal of Human Genetics, **56**, 1, 5-7.

[5] Guenther, C., Tasic, B., Luo, L., Bedell, M. and Kingsley, D. (2014) *A molecular basis for classic blond hair color in Europeans*. Nature Genetics, **46**, 7, 748-752.

[6] Han, J., Kraft, P., Nan, H., Guo, Q., Chen, C., Qureshi, A., Hankinson, S., Hu, F., Duffy, D., Zhao, Z., Martin, N., Montgomery, G., Hayward, N., Thomas, G., Hoover, R., Chanock, S. and Hunter, D. (2008) *A Genome-Wide Association Study Identifies Novel Alleles Associated with Hair Color and Skin Pigmentation.* PLoS Genetics, **4**, 5, e1000074.

[7] Genetics Home Reference, (2016). Is eye color determined by genetics?. [online] Available at: http://ghr.nlm.nih.gov/handbook/traits/eyecolor [Accessed 25/01/2016].

[8] Sturm, R. (2009) *Molecular genetics of human pigmentation diversity*. Human Molecular Genetics, **18**, R1, R9-R17.

[9] Sturm, R., Duffy, D., Zhao, Z., Leite, F., Stark, M., Hayward, N., Martin, N. and Montgomery, G. (2008) *A Single SNP in an Evolutionary Conserved Region within Intron 86 of the HERC2 Gene Determines Human Blue-Brown Eye Color*. The American Journal of Human Genetics, **82**, 2, 424-431.

[10] Abdel-Malek, Z. and Swope, V. (2011) *Epidermal Melanocytes: Regulation of Their Survival, Proliferation, and Function in Human Skin*. Melanoma Development, 7-33.

[11] McDevitt, D. (1982). *Cell biology of the eye.* (Academic Press), 200.

[12] Cichorek, M., Wachulska, M., Stasiewicz, A. and Tymińska, A. (2013) *Skin melanocytes: biology and development.* Advances in Dermatology and Allergology, 1, 30-41.

[13] AskNature, (n.d.). Rapid color change used for protection: cuttlefish. [online] Available at: http://www.asknature.org/strategy/346cbaa168e0f33cd4fc21a6d0cb50eb [Accessed 29/01/2016].

[14] Deravi, L., Magyar, A., Sheehy, S., Bell, G., Mathger, L., Senft, S., Wardill, T., Lane, W., Kuzirian, A., Hanlon, R., Hu, E. and Parker, K. (2014) *The structure-function relationships of a natural nanoscale photonic device in cuttlefish chromatophores*. Journal of The Royal Society Interface, **11**, 93, 20130942-20130942.

[15] Stuart-Fox, D. (2013). How do chameleons and other creatures change colour?. [online] Phys.org. Available at: http://phys.org/news/2013-05-chameleons-creatures-colour.html [Accessed 29/01/2016].

[16] Andouche, A., Bassaglia, Y., Baratte, S. and Bonnaud, L. (2013) *Reflectin genes and development of iridophore patterns in Sepia officinalis embryos (Mollusca, Cephalopoda).* Dev. Dyn., **242**, 5, 560-571.

[17] Kimura, T., Nagao, Y., Hashimoto, H., Yamamoto-Shiraishi, Y.-i., Yamamoto, S., Yabe, T., Takada, S., Kinoshita, M., Kuroiwa, A. and Naruse, K. (2014) *Leucophores are similar to xanthophores in their specification and differentiation processes in medaka*. PNAS, **111**, 20, 7343-7348.

[18] Uniprot, (n.d.). Paired box protein Pax-7. [online] Available at: http://www.uniprot.org/uniprot/P23759 [Accessed 29/01/2016].

[19] Farooqi, I. and O'Rahilly, S. (2006)*Genetics of Obesity in Humans*. Endocrine Reviews, **27**, 7, 710-718.

[20] Vaisse, C., Clement, K., Durand, E., Hercberg, S., Guy-Grand, B. and Froguel, P. (2000) *Melanocortin-4 receptor mutations are a frequent and heterogeneous cause of morbid obesity.* Journal of Clinical Investigation, **106**, 2, 253-262.

[21] Lango Allen, H., Estrada, K., Lettre, G., et al. (2010) *Hundreds of variants clustered in genomic loci and biological pathways affect human height. Nature*, **467**, 7317, 832-838.

[22] Trivellin, G., Daly, A., Faucz, F., et al. (2014) *Gigantism and Acromegaly Due to Xq26 Microduplications and GPR101 Mutation*. New England Journal of Medicine, **371**, 25, 2363-2374.

[23] Wikipedia, (2016). Robert Wadlow. [online] Available at: https://en.wikipedia.org/wiki/Robert_Wadlow [Accessed 03/02/2016].

[24] Wikipedia, (2016). Anna Haining Bates. [online] Available at: https://en.wikipedia.org/wiki/Anna_Haining_Bates [Accessed 03/02/2016].

[25] Wikipedia, (2016). André the Giant. [online] Available at: https://en.wikipedia.org/wiki/André_the_Giant [Accessed 03/02/2016].

[26] Wikipedia, (2016). Jorge González (wrestler). [online] Available at: https://en.wikipedia.org/wiki/Jorge_González_(wrestler) [Accessed 03/02/2016].

[27] Navarro, C. (2006) *Molecular bases of progeroid syndromes.* Human Molecular Genetics, **15**, 2, R151-R161.

[28] Hirschfeld, G., Berneburg, M., von Arnim, C., Iben, S., Ludolph, A. and Scharffetter-Kochanek, K. (2007). *Progeroid Syndromes*. [pdf] Deutsches Ärzteblatt. Available at: https://www.aerzteblatt.de/pdf/DI/104/6/a346e.pdf [Accessed 03/02/2016].

[29] Oren, D. (2002). *Accelerated Aging: Human Progeroid Syndromes*. [online] Encyclopedia.com. Available at: http://www.encyclopedia.com/doc/1G2-3402200013.html [Accessed 03/02/2016].