Effective Target Proteins for Skin-Whitening Based on Melanin Related Protein Network

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1. Introduction

In Korea, 55% of women are interested in facial blemishes and 62.50% of women were experienced in using skin whitening cosmetics [1]. A lot of cosmetic manufactories are selling many kinds of skin whitening cosmetics to come up to consumer's expectations. Skin-whitening cosmetics inhibit to get freckled or make to lighten skin tone by lessening the concentration of melanin. Thus, the principle of skin whitening cosmetics is inhibition of melanin synthesis.

Melanin is synthesized in melanosome that is responsible for color and photoprotection as an organelle. Six melanosome-specific proteins, MLANA, TYR, TYRP1, DCT, GPR143, PMEL17 are essential to melanin synthesis [2-3]. We obtained six proteins and their interacting proteins from STRING (http://string-db.org) and made melanosome-specific protein interaction bipartite network using Cytoscape (http://www.cytoscape.org/). From the network, we hope to predict that effective target proteins inhibit to melanin synthesis.

2. Prediction of target protein based on modular structure

Figure 1 shows the melanosome-specific protein interaction bipartite network that contains 41 proteins as two different nodes (gray and white nodes indicate six melanosome-specific proteins and their interacting proteins, respectively) and their interactions. We extracted two modules from the bipartite network by using MCODE in the cytoscape program [4 and Figure 2]. A module structure is generally considered to be a group of nodes that are densely connected amongst each other but loosely connected to other nodes outside the module [5]. Six specific proteins are distinctly separated to the two modules.
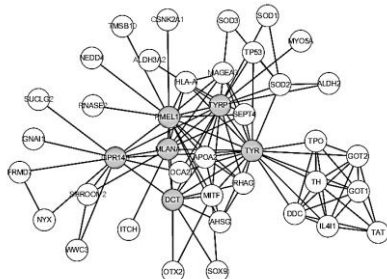

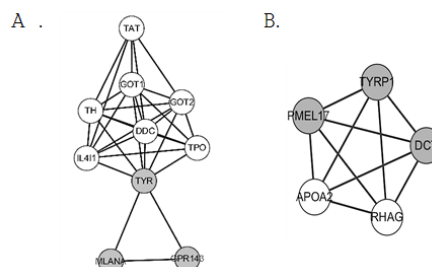Figure 1. Melanosome- specific protein-protein network

Figure 2. Modular structures

Next, we removed the three proteins, TYR, MLANA, and GPR143 in the bipartite network and obtained only reduced network [Figure 3A]. We also obtained the reduced network by removal of three different proteins, PMEL17, TYRP1, and DCT using same method [Figure 3B]. One reduced network contains 24 nodes [Figure 3A] but the other reduced network contains 32 [Figure 3B]. By considering reduced network size, three proteins from the modular structure A in Figure 2 will be effect targets to skin-whitening rather than those from the modular structure B. Practically, inhibitor of the TYR that predicted as an effective target protein in this study has widely been using as cosmetic material for most skin-whitening cosmetics. If we simultaneously use three inhibitors of the TYR, MLANA, and GPR143 target proteins as cosmetic materials for skin-whitening, it can more effectively control to melanin synthesis.
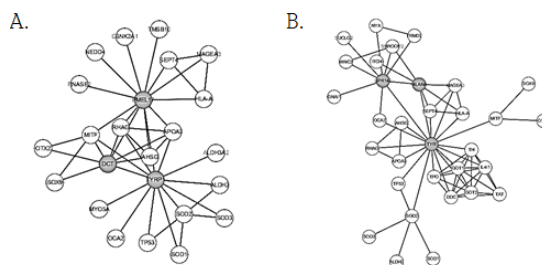
Figure 3. Reduced networks obtained by remove of core proteins from modular structures in Figure 2

[Table 1] Possible inhibitors of effective target protein

Target protein	Inhibitor
TYR	Arbutin, Aloesin, Anisic acid, Kaempferol, Cumicacid
TYRP1	Tyrostat, Tocopherol, Gastrodia elata
MLANA	Wnt5a, Rengyolone

3. Conclusion

In this study, we focused on how to regulate melanin synthesis effectively based on the melanosome-specific proteins network and identified highly effective target proteins for skin-whitening. When we approached to modular structure of the network, effective target proteins will be TYR, MLANA, and GPR143. However, PMEL17, TYRP1, and DCT will also be useful candidates although TYR, MLANA, and GPR143 are more effective based on modular structural information.

We can obtain specific inhibitors of melanin synthesis from natural substances and chemical compounds for skin-whitening, but they possibly induce side-effect or unpredicted by-product during development of the cosmetics. It is possible to suggest several different combinations of inhibitors from our target protein candidate information when we confront unexpected difficulty such as side-effect and by-product during development of the cosmetics [Table 1 and 6-9]. In this study, we provide effective information about development of skin-whitening cosmetics and also provide insight to selection of the effective targets as deriving the modular structural information from the complex network.

4. References

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