

FINAL PROGRESS REPORT

Hee-Young Park, Ph.D.
Associate Research Professor
Departments of Dermatology and Biochemistry
Boston University School of Medicine

Layman's Report

1. A Brief Background

Vitiligo, a skin disease with an irregular-sized loss of skin pigment, has a devastating impact on the social and psychological well-being of an individual, as well as lack of sun-protection within the affected depigmented areas. The causes for the loss of skin pigment are not well understood. One of the factors that have been implicated to be important in causing the death pigment producing cells, termed melanocytes, is the presence of molecules released by the local or micro-environments, specifically keratinocytes that stresses the survival of pigment cells.

2. Objective of the Study

Bone-Morphogenetic Protein-4 (BMP-4) is a small molecule synthesized and released by both melanocytes and neighboring skin cell types called keratinocytes. The released BMP-4 then influences the biology of melanocytes. BMP-4 was shown to reduce the synthesis of melanin in melanocytes and was implicated to be important for the survival of melanocytes. Excess release of BMP-4 by keratinocytes may harm and reduce the survival of melanocytes. The goal of the proposed studies were to examine how BMP-4 reduces the synthesis of melanin and the survival of melanocytes.

3. Results Obtained

- During the first part of the project, we used primary human melanocyte cultures derived from newborn foreskins to demonstrate that exogenous addition of BMP-4 to melanocyte cultures reduced the protein levels of tyrosinase related protein-1 (TRP-1), Melan-A/MART-1, protein kinase C- β (PKC- β), MC1R and BCL2. These proteins are critical for melanin synthesis, and survival of melanocytes. Therefore, decreased levels of these proteins by BMP-4 would result in a lower amount of melanin and increased susceptibility to damages.
- During the second phase of our study, we examined whether keratinocytes within the vitiligo lesions produce excessive level of BMP-4 when compared to the level found in normal keratinocytes using vitiligo skin biopsies of lesional and perilesional areas. The results obtained to date showed a tendency for increased level of BMP-4 in the lesional area. We are currently staining higher number of donors to perform statistical analysis.

4. Significance of the Results to Vitiligo

Our results demonstrate that BMP-4 can have a significant impact on the survival of melanocytes. Reduced level of eumelanin by BMP-4 in melanocytes would increase the susceptibility of melanocytes to DNA damages caused by UV or other genotoxic agents. Moreover, reduction in the level of anti-apoptotic protein Bcl2 would likely to lessen the chance of melanocytes to survive in response to UV or

other conditions that may be stressful to melanocytes. Moreover, in vivo staining indicates that the level of BMP-4 is elevated in lesional areas of vitiligo.

5. Plans for Future

These results will be compiled and submitted for a publication. We expect two publications from these studies. The National Vitiligo Foundation will be properly acknowledge for support of the work.

Scientific Report

During the past six months of the funding period, my laboratory, in collaboration with Dr. Kang at Ajoo University School of Medicine, has focused on whether the level of BMP-4 is elevated in the lesional area of vitiligo biopsies when compared to adjacent normal areas.

For these studies, a library of vitiligo biopsies and adjacent normal skins stored in paraffin block were used. Monoclonal antibody specific to BMP-4 was purchased from Cell Signaling, Inc. and the optimal concentration of antibody for the immunostaining was determined. Then, paired normal and lesional sections were immunostained for BMP-4. Photos were taken. Image analysis will be performed for statistical analysis.