

# IMMUNE AND INFLAMMATORY GENE EXPRESSION PROFILES OF CHRONOLOGICAL (INTRINSIC) SKIN AGING AND PHOTO-AGING

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## INTRODUCTION

Skin aging involves many functional and structural changes that evolve over time, and are influenced by environmental insults, particularly UV light (1). Descriptive research (e.g., histopathology) has characterized many structural changes associated with chronological skin aging and photo-damage (2). However, genomics and bioinformatics capabilities enable a more comprehensive assessment of these processes at the fundamental level of gene expression.

## OBJECTIVE

To examine baseline gene expression patterns in sun-protected and sun-exposed skin from young and aged women.

- Compare gene expression differences across subjects and across UV protected and UV exposed skin sites.
- Identify key biological themes associated with skin aging.
- Assess relevance of immune & inflammatory response to skin aging process at level of gene expression.

## METHODS

Biopsies were obtained from UV exposed skin (outer forearms) and UV protected skin (buttocks) from ten 18-20 yr. and ten 60-67 yr. female subjects (latter with moderate-severe photodamage).

- Target cDNA (from extracted mRNA) hybridized to Affymetrix U133 Plus 2 microarrays (54,613 probes).
- Statistically analyzed data filtered by significance ( $p < .05$ ) and fold changes and resulting gene lists queried for most differentially regulated genes associated with skin aging.
- Skin aging-associated biological themes identified by analysis of over-represented gene ontology terms.

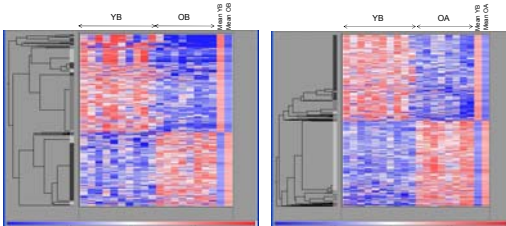
Digital images of biopsy sites show texture and pigmentation changes indicative of chronological aging (YB vs. OB) or chronic photo-aging (YB vs. OA, YA vs. OA, OB vs. OA).



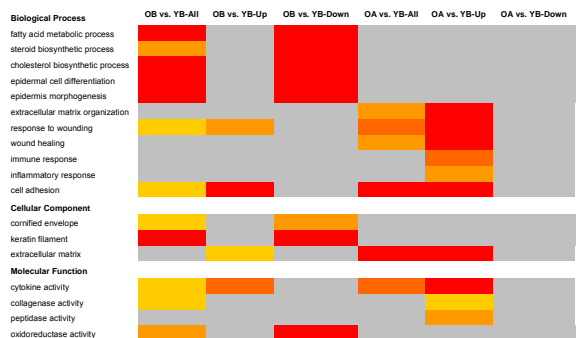
# Significant Gene Changes: (# By Chance =  $54,613 \times .05 = 2731$ )  
 Chronological Aging (YB vs. OB): 7215  
 Photo-Aging (YB vs. OA): 9930  
 Photo-Aging (YA vs. OA): 13,640  
 Photo-Aging (OB vs. OA): 11,216

## RESULTS

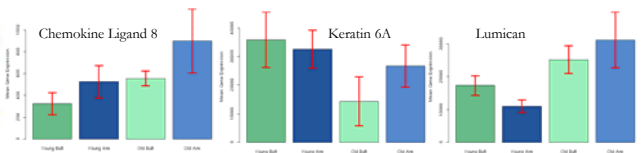
Heatmaps of Up-regulated (red) and down-regulated (blue) genes representing chronological aging (YB vs. OB) and one of three comparisons representative of photo-aging (YB vs. OA). Columns represent individual subjects and rows represent individual genes (probes). Genes were selected based on positive expression, significant differential expression ( $p < .05$ ) and  $\geq 50\%$  differential expression. Numbers of individual genes (probes) meeting these criteria for each comparison were: YB vs. OB: 897; YB vs. OA: 2074.



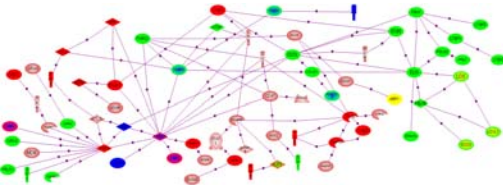
Biological themes emerging from the OB vs. YB and OA vs. YB site comparisons were identified by statistical analysis of over-represented gene ontology terms associated with the differentially regulated genes vs. all genes expressed in the study. Increasing significance for each listed term is indicated by yellow  $\rightarrow$  red color. Chronological aging (OB vs. YB) was uniquely associated with down-regulation of epidermal differentiation processes. Up-regulation of processes related to immunity/inflammation were seen in both comparisons but were most significant in the photo-aging (OA vs. YB) comparison.



Raw data for representative genes regulated in chronological skin aging and photo-aging.



Biological interaction network (direct protein binding) created from genes up-regulated in photo-aged skin (OA vs. YB) by use of pathway mapping software (Pathway Studio 5.0<sup>TM</sup>) and its natural language processing of protein-protein interactions derived from all of PubMed. Proteins with biological functions related to inflammation (red), extracellular matrix (green), protease activity (blue), oxidoreductase activity (yellow), and combinations thereof, are colored to indicate numerous protein-protein interactions within and across those themes.



## CONCLUSIONS

The immune/inflammatory response was the dominant theme at gene expression level in both chronological aging and photo-aging.

- Linked to other important themes (e.g., extracellular matrix, protease activity, oxidoreductase activity).
- Differences were noted between chronological aging and photo-aging in sub-themes and specific genes; though generally, gene expression changes noted in chronological aging were similar (but enhanced) in photo-aging.
- Biological pathways interconnecting themes may suggest new insights into skin aging and ways to combat it.

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## REFERENCES:

1. GJ Fisher, et al., Arch. Dermatol., 138:1462-1470, 2002.
2. M El-Domyati, et al., Exp. Dermatol., 11:398-405, 2002.

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