Characterization of Actinic Lentigines from Japanese Subjects and Comparison with Lesions from Caucasians

INTRODUCTION

Actinic lentigines (AL), also called lentigo senilis or solar lentigines, are benign skin hyperpigmented lesions associated with age and chronic sun exposure (1,2). Despite the high prevalence of pigmented spots in elderly people, particularly in Asian populations (3), the biological events underlying the development of these lesions remain unclear.

In this study, we characterized a clinically homogenous group of AL from Japanese volunteers through morphological and gene expression profiling analysis. Transcriptomic data were then compared to previous data obtained from European volunteers, in order to better understand the pathophysiological characteristics of AL in both populations.

MATERIALS AND METHODS

1. Volunteers:
20 Japanese women, aged 54-71, phototype II-IV, were included in the Japan study (12 for transcriptomic analysis and 8 for morphological analysis of AL). 15 Caucasian women aged 51-67 years, phototype I-II were included in the Europe study.

2. AL Selection:
AL from the dorsolateral side of the hands were selected through dermatoscopic imaging (DGI) magnification (Fotofinder dermoscope™, DermoScience) and pigmented pattern scoring. Dedicated software was designed to assess, within the lesion, the epiluminescence index (EI) and the undulation index (UI) of melanocytes (4). Only AL with an EI over 0.7 (i.e. containing a majority of elongated patterns) were included. In this range, the epiluminescence index was significantly correlated with the degree of deformation of the dermal-epidermal junction (DEJ) (4).

3. Processing of biopsies:
Pairs of 3 mm biopsies were taken from each volunteer, one biopsy from the AL lesion and another one from an adjacent non-lesional (NL) skin area. One set of biopsies was processed for histology (HES) and Fontana-Masson (FM) staining and the other set for RNA extraction and gene expression profiling using Affymetrix® U133A 2.0 chips.

4. Bioinformatics and statistical analysis:
Raw data were normalized using the Robust Multi-chip Average method. Unsupervised analysis and clustering were performed using a Non-negative Matrix factorization (NMF) approach, and supervised differential analysis was performed using a T-test linear model. Genes were considered to be differentially expressed between AL and NL biopsies when fold change (FC = AL/NL) was >1.5 for up-regulated genes or < -1.5 for down-regulated genes, with a p-value < 0.05.

RESULTS

MORPHOLOGICAL ANALYSIS OF AL FROM JAPANESE VOLUNTEERS

Advanced AL from Japanese volunteers displayed alterations of the whole skin structure, illustrated by the differential expression of more than 200 genes involved in multiple biological functions – including extracellular matrix organization, inflammation and immune response and epidermal proliferation and differentiation. Comparison of Japanese and European AL signatures showed that AL lesions selected on the same clinical criteria (EI >0.7) in both populations (5) share a common gene expression profile which manifests itself in multiple discrete areas in both the AL compartments, apart from the melanocyte itself, and suggests that AL lesions have to be considered globally, and not only through the prism of melanocytes. These findings should be taken into account in the development of an efficient long-term treatment of age spots.

COMPARISON OF EUROPEAN AND JAPANESE AL SIGNATURES

CONCLUSION


REFERENCES


2. T-test linear model. Genes were considered to be differentially expressed between AL and NL biopsies when fold change (FC = AL/NL) was >1.5 for up-regulated genes or < -1.5 for down-regulated genes, with a p-value < 0.05.