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BIOINFORMATICS FACILITATE HAPLOTYPE ANALYSIS IN PSORIASIS

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Abstract. Psoriasis is an inflammatory skin disease. Vitamin D is successfully used for psoriasis therapy. Polymorphisms and haplotypes in the VDR gene may explain the differences in response to vitamin D therapy. We study vitamin d receptor gene polymorphisms in 100 psoriasis patients and 100 control subjects. We have detected SNPs by PCR-RFLP and analyze by CHAPLIN. We found statistically significant allele genotype and haplotype in patients.

Keywords: skin, PCR-RFLP, bioinformatics facilitate haplotype analysis, psoriasis.

Introduction. Psoriasis is an inflammatory disease characterized by increased squamous cell proliferation (grow faster than your body can remove, or shed, them) and impaired differentiation (figure 1) (1,2)

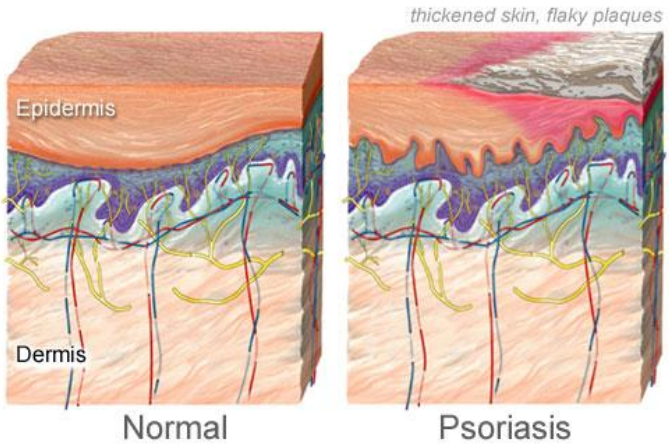


Figure 1. Histologic changes in psoriasis

Lesions usually show up on your scalp, elbows, knees, and lower back (figure 2).

Psoriasis is not a congenital or contagious, etiology of the disease is multifactorial, non mendelian (non one gene-one protein-one disease). Although major component of the etiology is genetic predisposition, there is no one gene and mutation to cause disease. Rather one or more association with a few gene polymorphisms. Psoriasis is not congenital or contagious. Certain triggers such as

environmental (allergens, bacteria, cosmetics) or intrinsic (chronic inflammatory diseases) in predisposable person start disease anyway (figure 3) (1,2).

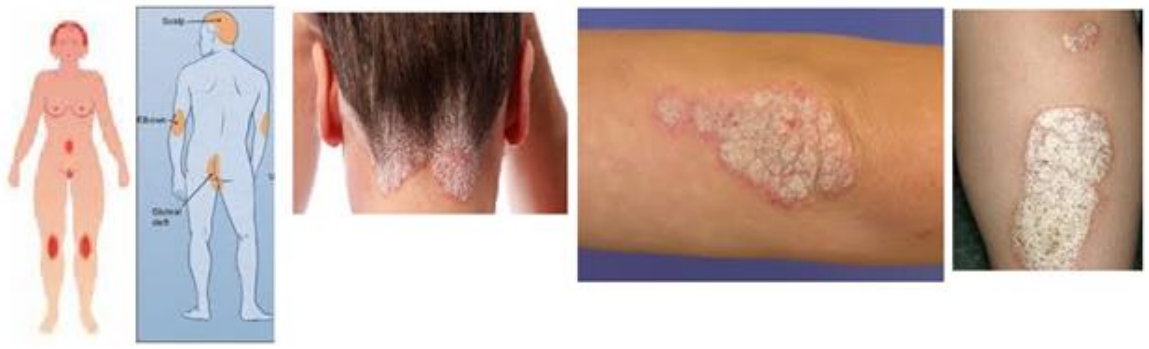


Figure 2. Locations of the lesions on body

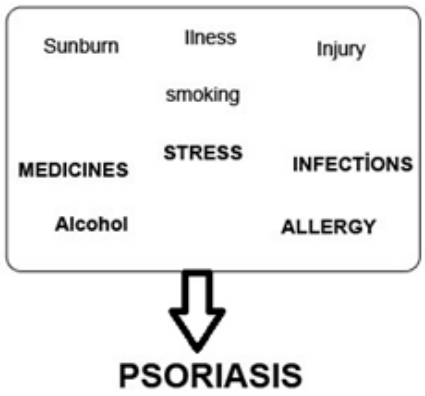


Figure 3. Triggers of Psoriasis

According to WHO 2016 “Global Report on Psoriasis” affects men and women of all ages, in all countries, prevalence of psoriasis in countries vary between 0.09% and 11.4%. because of registration of psoriasis cases is not compulsory, reliable data about prevalence are difficult to find. There are no clear climate differences in prevalence, in Norway bigger than 5%, in Australia near 5%, in UK 2%. Trend changes in incidence/prevalence of disease is difficult, it seem like slowly increasing (3).

Disease is not fully curable. Vitamin D3 and its analogs are use in treatment successfully, However some patients do not. We aimed to compare the allele and genotype frequencies of Vitamin D Receptor Gene genotypes and haplotypes in psoriasis patients and healthy controls, and to determine the association with response to vitamin D therapy (4).

Method. Total of 102 psoriasis patients and 102 controls are studied. Cases were divided two subgroup as calcitriol treatment and PASI score evaluated.

Four SNPs of the VDR gene was determined by PCR RFLP (Apa I, Bsm I, Fok I and Taq I) .

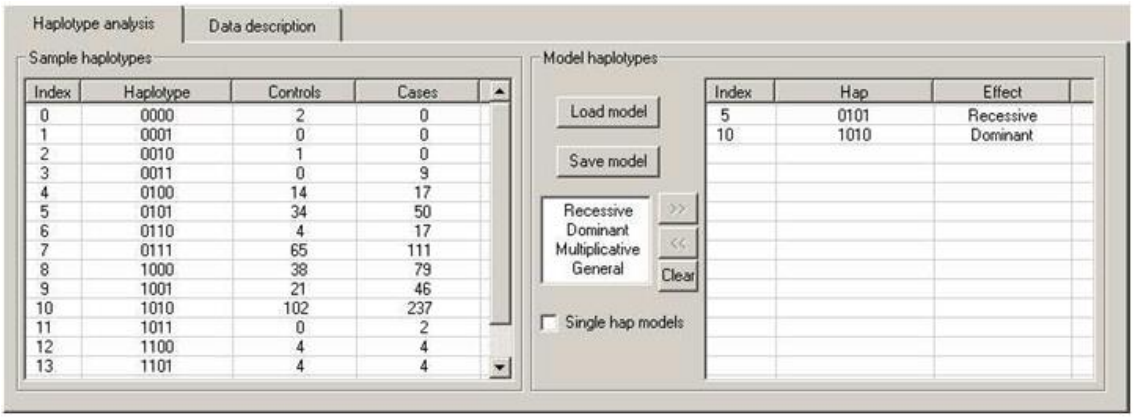
Haplotype and statistical analysis. Allele frequencies were calculated from genotype frequencies based upon Hardy-Weinberg equilibrium;

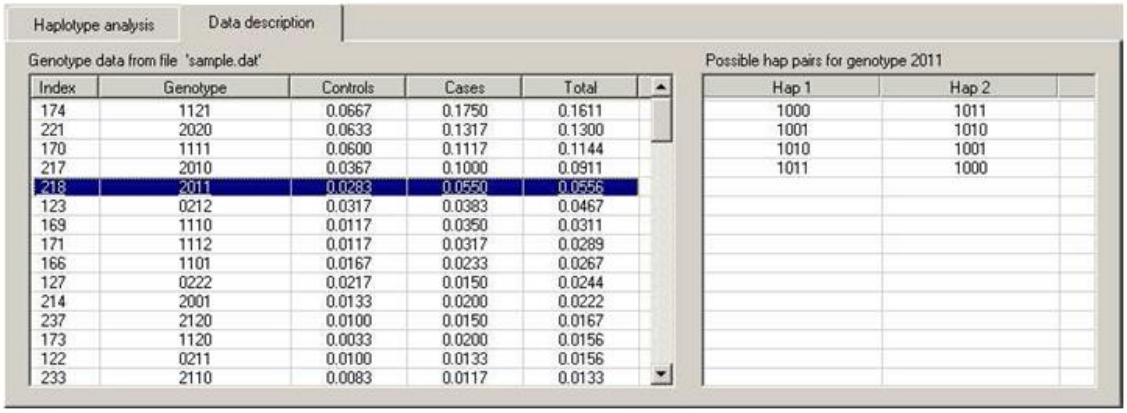
p, q: allele frequency, *p2, q2, 2pq*: genotype frequency.

$$p+q=1 \tag{1}$$

$$(p_2)+(2pq)+(q_2)=1.$$

Haplotype analysis was done by CHAPLIN1.2 (7,8)





Result

-Allele frequency of T and genotype frequency of Tt was significantly higher in patients than controls (p values 0.038 and 0.04, respectively).

-The Aa and bb genotypes were significantly higher in early onset than late onset psoriasis (p values 0.008 and 0.04, respectively).

-The genotype Ff was significantly higher in non-responders, while ff and TT were significantly lower in non-responders to the vitamin D3 therapy (p values 0.04, 0.0001, 0.009, respectively).

The significance of the Wald and LR statistics p=0.0042 suggesting that FfBbAatt is a disease-susceptibility haplotype.

Discussion. The data related to VDR polymorphisms and psoriasis is very limited in the literature when compared with other situations such as bone mineral density, diabetes and cancers.

Recent years personal medicine become very popular and polymorphisms (VDR and more gene) have importance for medical therapy and diet.

However in bioinformatic perspective its need improvements for several points. Programs must be user friendly.

-In institution we need programs that non-commercial/academic license.

-Programs can be executable in multiplatform, do not need special operating system such as Unix, linux.

-Input must be ordinary format (txt, xls) and capacity can be large scale (thousand data per file).

-Estimation algorithm must be clear, proofed and acceptable for many author, editor, referee.

-Output also must be ordinary format and can be understandable from standard molecular biologist.

-It has easy and familiar interphase, as possible as free from command line.

-Working files can be convertible to common formats.

End- final users generally have limited knowledge and experience about algorithm and principles about programs that they want to use. These users concentrated on their profession working area, as DNA-RNA-protein isolation from biological samples, analytic reaction, identification, grant proposals and manuscript writing and most important build association and hypotesis.

Nowadays almost all study output need bioinformatical analysis in different complexity from relatively simple genotip-haplotype analysis to association of raw microRNA array data with functional target protein and biological pathway. Hence noncommercial, working on ordinary familiar desktop environment, user friendly end user programs facilitates and increase the new discoveries and human and earth life.

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References

[1]. www.webmd.com/skin-problems-and-treatments/psoriasis

[2]. Jordan CT, Coa L, Roberson EDO et al: PSORS2 is Due to Mutations in CARD14. Am J Hum Genet, 2012; 90: 784–95

[3]. Global report on psoriasis, WHO Library Cataloguing-in-Publication Data, 2016, ISBN 978 92 4 156518 9.

[4]. Halsall JA, Osborne JE, Pringle JH, Hutchinson PE: Vitamin D receptor gene polymorphisms, particularly the novel A-1012G promoter polymorphism, are associated with vitamin D3 responsiveness and non-familial susceptibility in psoriasis. Pharmacogenet Genomics, 2005; 15: 349–55.

[5]. Carling T, Ridefelt P, Hellman P et al: Vitamin D Receptor Polymorphisms Correlate to Parathyroid Cell Function in Primary Hyperparathyroidism. J Clin Endocrino Metab, 1997; 82: 1772–75

[6]. Harris SS, Eccleshall R, Gross C et al: The Vitamin D Receptor Start Codon Polymorphism (FokI) and Bone Mineral Density in Premenopausal American Black and White Women. J Bone Miner Res, 1997; 12: 1043–48

[7]. M.P. Epstein and G.A. Satten. Inference on haplotype effects in case-control studies using unphased genotype data. Am. J. Hum. Genet., 73:1316-1329, 2003.

[8]. Duncan R.D., EpsteinM.P., Satten G.A. Case-Control Haplotype Inference (CHAPLIN). Version 1.2, September 2006.