

## Retraction: Ana Strezova. Genotyping of HLA-A, HLA-C and HLA-B Loci with Reverse Line Strip Hybridization in Macedonian Population and Association of HLA Class I Alleles with Spondilitis [MSc thesis]

Mirko Spiroski

*Institute of Immunobiology and Human Genetics, Faculty of Medicine, Ss Cyril and Methodius University, Skopje, Republic of Macedonia*

### Abstract

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**Key words:** retraction; Master of Science thesis; scientific fraud; Republic of Macedonia.

**Correspondence:** Mirko Spiroski, MD, PhD. Institute of Immunobiology and Human Genetics, Faculty of Medicine, University "Ss Kiril and Metodij", 1109 Skopje, PO Box 60, Republic of Macedonia. E-mail: mspiroski@yahoo.com

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**Aim.** The aim of this report is to retract the results of Ana Strezova submitted without permission of her mentor and her institution for Master of Science (MSc) degree at the Faculty of Medicine, University "Ss Cyril and Methodius", Skopje, Republic of Macedonia.

**Material and Methods.** Two populations were published from the same cohort: i) in the 15th International Histocompatibility and Immunogenetics Workshop 250 samples for HLA-A, 247 samples for HLA-B, 250 samples for HLA-C, 564 samples for HLA-DRB1, and 213 samples for HLA-DQB1 were included; and ii) in retracted MSc degree 250 samples for HLA-A, HLA-B and HLA-C were included.

**Results.** HLA DNA typing results from Macedonian population were officially submitted for analysis and publication to the 15th International Histocompatibility and Immunogenetics Workshop (IHIWS). Results were prepared and submitted for publication in *Tissue Antigens* (received 7 July 2009; revised 12 January 2010; accepted 1 February 2010). Ana Strezova without permission of her mentor and director of the Institute of Immunobiology and Human Genetics submitted MSc thesis for defence with the identical results as in submitted manuscript. A total number of 5 HLA genes and 220 alleles are published by the 15th International Histocompatibility and Immunogenetics Workshop in comparison with 3 HLA genes and 58 alleles in retracted MSc thesis.

**Conclusion.** The results of the MSc thesis of Ana Strezova with the title "Genotyping of HLA-A, HLA-C and HLA-B Loci with Reverse Line Strip Hybridization in Macedonian Population and Association of HLA Class I Alleles with Spondilitis" are retracted because: i) the content was already submitted for publication; ii) the statistical methods are inappropriate for ambiguous resolution of the data; and iii) the permission was not allowed by her mentor and director. Editors-in-Chief and employers are advised to be aware of possible acceptance of this thesis and the results submitted in the future for publication.

### Introduction

Two types of difficulty may arise when authors are reporting work. First, errors may be noted in published articles that require the publication of a correction or erratum on part of the work. The second type of difficulty is scientific fraud. If substantial doubts arise about the honesty or integrity of work, either submitted or published,

it is the editor's responsibility to ensure that the question is appropriately pursued, usually by the authors' sponsoring institution. Ordinarily it is not the responsibility of the editor to conduct a full investigation or to make a determination; that responsibility lies with the institution where the work was done or with the funding agency. The editor should be promptly informed of the final decision,

and if a fraudulent paper has been published, the journal must print a retraction [1].

Retraction is a mechanism for correcting the literature and alerting readers to publications that contain such seriously flawed or erroneous data that their findings and conclusions cannot be relied upon. Unreliable data may result from honest error or from research misconduct. Retractions are also used to alert readers to cases of redundant publication (i.e. when authors present the same data in several publications), plagiarism, and failure to disclose a major competing interest likely to influence interpretations or recommendations. The main purpose of retractions is to correct the literature and ensure its integrity rather than to punish authors who misbehave [2].

Since 2007, English abstracts of Master of Science (MSc) theses defended at the Faculty of Medicine in Skopje and deposited in the Central Medical Library, are regularly published in Macedonian Journal of Medical Sciences [3, 4].

The aim of this report is to retract the results of Ana Strezova submitted without permission of her mentor and her institution for MSc degree at the Faculty of Medicine, Ss Cyril and Methodius University, Skopje, Republic of Macedonia and inform the biomedical scientific community.

## Material and Methods

During the 15th International Histocompatibility and Immunogenetics Workshop (IHIWS), 14 human leukocyte antigen (HLA) laboratories participated in the Analysis of HLA Population Data (AHPD) project (including Macedonian population). The main goals of the AHPD project were: (i) to estimate frequencies by taking into account ambiguous genotypic data, (ii) to test for Hardy-Weinberg equilibrium (HWE) by using a nested likelihood ratio test involving a parameter accounting for HWE deviations, (iii) to test for selective neutrality by using a resampling algorithm, and (iv) to provide explicit graphical representations including allele frequencies and basic statistics for each series of data. Institute of Immunobiology and Human Genetics, Faculty of Medicine at the University "Ss Cyril and Methodius" in Skopje was registered and participated in the 13-15 International Histocompatibility and Immunogenetics Workshops (IHIWS). HLA DNA typing results from Macedonian population were submitted for analysis and publication to the 15th International Histocompatibility and Immunogenetics Workshop (IHIWS). Results were prepared and submitted for

publication in Tissue Antigens (Received 7 July 2009; revised 12 January 2010; accepted 1 February 2010) [5].

Ana Strezova (MD) was employed at the Institute of Immunobiology and Human Genetics since 2001 and was involved in HLA DNA typing. In September 2009 she asked for three months of uncovered holiday and left the Republic of Macedonia. In the same time (September 2009 - two months after submission of our manuscript to Tissue Antigens [3]) Ana Strezova without permission of her mentor and director of the Institute of Immunobiology and Human Genetics (prof. Dr. Mirko Spiroski) submitted MSc thesis for defence using the identical results as in submitted manuscript to Tissue Antigens [6].

As a mentor and as a director I informed the Dean's Office for the unethical act of Ana Strezova and proposed withdrawal of the MSc thesis because: i) the content was already submitted for publication; ii) the statistical methods are inappropriate for ambiguous resolution of the data; and iii) the permission was not allowed by her mentor and director. Irrespective of that, Ana Strezova did not withdraw MSc thesis and on December 04, 2009 (without her mentor and without anybody of the Institute of Immunobiology and Human Genetics) she presented the data. Immediately after defence she permanently left the Institute of Immunobiology and Human Genetics and her country of origin Republic of Macedonia.

While the population samples, genomic DNA isolation and HLA genotyping were the same for the 15th IHIWS submission and the retracted MSc thesis [7-11], different statistical analyses were used. In the 15th International Histocompatibility and Immunogenetics Workshop Single population statistical analyses were performed using the GENE[RATE] tools [9, 10], while in the retracted MSc degree the statistical analysis was performed by using the Arlequin Software version 2.000 [12].

## Results

HLA DNA genotyped results from our laboratory were included in the analysis of the HLA population data (AHPD) submitted to the 15th International Histocompatibility/Immunogenetics Workshop by using the GENE[RATE] computer tools accommodating ambiguous data (AHPD project report) and are published [5].

In the "Single population analyses" of the paper allele frequencies and basic statistics, treatment of ambiguities, test for Hardy-Weinberg equilibrium, and test

for selective neutrality, were published given in four or more digits. In the "Population comparisons" of the paper African, American, and European populations (including Macedonian population) were compared [5].

Comparison between the HLA DNA genes and alleles in Macedonian population submitted and published by the 15th International Histocompatibility and Immunogenetics Workshop and the similar results published in retracted MSc thesis are shown in Table 1.

**Table 1: Comparison between the HLA DNA genes and alleles in Macedonian population submitted and published by 15th International Histocompatibility and Immunogenetics Workshop and the same results published in retracted MSc thesis.**

	HLA genes	Identified HLA alleles					Total
		HLA-A	HLA-B	HLA-C	HLA-DRB1	HLA-DQB1	
15th IHIWS*	5	46	62	33	74	5	220
Retracted MSc	3	16	29	13	0	0	58

\*, 15th International Histocompatibility and Immunogenetics Workshop; MSc, Master of Science thesis.

A total number of 5 HLA genes and 220 alleles in Macedonian population are published by the 15th International Histocompatibility and Immunogenetics Workshop in comparison with 3 HLA genes and 58 alleles in retracted MSc thesis.

In the retracted MSc thesis HLA-A, HLA-B, and HLA-C frequencies in Macedonian population are given with two digits (allele groups) and gene and allele ambiguities are not solved. Association between HLA-A, HLA-B, and HLA-C and spondylitis were calculated with two digits without solution of gene and allele ambiguities [6].

## Discussion

In this report retraction of the results from the MSc degree of Ana Strezova is announced, which was submitted and defended without permission of her mentor and her institution. The author and authorities at the Faculty of Medicine in Skopje were informed in detail about the reasons for withdrew of the MSc thesis, but they did not respond positively.

Furthermore, there are a lot of significant differences between the results for Macedonian population analysed and published by the 15th International Histocompatibility and Immunogenetics Workshop [5] and the results in retracted MSc thesis [6]. These differences had tremendous impact on the frequencies of the HLA-A, HLA-B, and HLA-C alleles with erroneous frequencies in the retracted MSc thesis. The conclusions

drawn from the data of the association between HLA and spondylitis in the retracted MSc thesis are therefore erroneous and invalid. More precisely, all results in the retracted MSc thesis are scientific fraud and could not be used for any comparisons or analyses.

Scientific fraud can divert the search for truth, and it pollutes the record of that search, that is, the scientific literature. Once someone identifies an article as fraudulent, the scientific community has 2 duties: 1) to warn scientists to ignore the article and 2) to prevent further pollution by scientists who inadvertently cite the article [13].

It is obvious that Ana Strezova did not accept withdrawal of the MSc thesis after oral and written suggestion to do so by her mentor and director, because she decided to left Institute of Immunobiology and Human Genetics and her country of origin Republic of Macedonia. But publication ethics and responsibilities are universal and those responsibilities lie within the institution where the work was done - Institute of Immunobiology and Human Genetics in this case [1].

In the Republic of Macedonia this is the first retraction of MSc thesis and probably first retraction in the biomedical field. Biomedical institutions, biomedical journals and biomedical scientists (authors) from the Republic of Macedonia are not familiar with the publication ethics [14] and probably because of that they did not recognise and prevented unethical submission and fraudulent defence of MSc thesis.

The mentor and institution apologize for any inconvenience that this may have caused the scientific community and readers of the retracted MSc thesis.

In summary, the results of the MSc thesis of Ana Strezova with the title "Genotyping of HLA-A, HLA-C and HLA-B Loci with Reverse Line Strip Hybridization in Macedonian Population and Association of HLA Class I Alleles with Spondylitis" are retracted because: i) the content was already submitted for publication; ii) the statistical methods are inappropriate for ambiguous resolution of the data; and iii) the permission was not allowed by her mentor and director. Editors-in-Chief and employers are advised to be aware of possible acceptance of this MSc thesis and the results submitted in the future for publication.

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