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- Military application of genetics with special respect to personal identification -

Doctoral (PhD) thesis and official reviews

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Consultant:

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DESCRIPTION OF THE SCIENTIFIC PROBLEM

The military application of scientific observations and research results has always characterized the history of the modern man. Numerous examples can be listed from the use of primitive flint-flakes in the stone age through bronze age weapons manufacturing and medieval war machines to the military application of the results of the 19th-20th century global scientific-technical revolution. The majority of inventions, tools, machines and later more complicated processes and technology based on the proven laws of nature necessarily led to military applications due to their inherent efficiency. In possession of them or information on them could lead to a more successful fight against the current enemy, more successful battles and conquering wars, furthermore, the possession of these tools, methods and technologies proved to be a protective shield if needed thanks to the power of deterrence.

Initially, this development was rather limited by the ingenuity of the human mind than the absence, character, quality and quantity of financial resources needed for realization. As a result of the development of science and technology including technologies based on the achievements of natural sciences, basic and applied research became more and more expensive. The need for more powerful, more deterrent and perfect technologies including technologies for special military purposes made the representatives of the prevailing power interested in directly or indirectly participating in the development of these technologies by restructuring and concentrating mental and financial resources. The first prominent examples for this phenomenon can be found in the period right before and during World War II.

It is a well-known historical fact that the German rocket technology research and development centre led by Werhner von Braun was founded in Peenemünde in 1937. In 1943, Franklin Delano Roosevelt, the then president of the United States of America (USA) ordered the establishment of the *Los Alamos National Laboratory (LANL)* as part of the so-called Manhattan Project for the production of the atomic bomb. The development of natural sciences in the 20th and 21st centuries have necessitated the concentration of scientific, venture and significant military financial resources similarly to *Losalamos* in three further areas that can be well distinguished based on their character and significance.

The first area comprises IT and communication-technological basic and applied research starting from the 1950s. As a result, space research started to develop partly on its own with the establishment of NASA in the USA on 1st October, 1958 and Bajkonur in the Soviet Union a year earlier. Furthermore, so-called *silicon valleys* were established in the world-leading industrial countries with the most developed research and innovation based on the most important IT research, in the process of which LANL played one of the leading parts from the 1950s; however, its role was gradually taken over by *Silicon Valley* established around the Stanford University of San Francisco (California, USA) with its centre in San Jose. A similar concentration of financial resources started in Asia, first in Japan with the centre located in Tokio since the 1960s then in South-Korea in Seoul since the 1970s, while in China it started in the Haidian district of Beijing in the *Zhongguancun Scientific and Technological Zone* in the 1980s. The silicon valley of the Middle East was founded in the middle of the 1990s and the construction of the first Russian silicon valley started in 2010 in Skolkovo, the south-west district of Moscow (Skolkovo IT Cluster). In the European Union, subsidies remained limited to the level of the member states and the development of the IT sector was realized through a kind of specialization. Finland, Sweden, the Netherlands, France and Germanyhave become the beneficiaries of these innovations since the 1990s and achieved a

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global impact through their national companies (e.g. Nokia, Ericsson, Philips, Alstom, Siemens).

The second concentration of resources was realized by promoting the military application of biotechnological research and its results. Research on biological and toxic weapons in the last decades of the previous century represented the secret or – balancing on the verge of international law – relatively open military applications of these results. By the millennium – partly because of the international conventions prohibiting the production and experimental application of these weapons – several biotechnological inventions were no longer used as weapons but to achieve a better combat preparedness of the army, to increase the physical skills of trained soldiers, to increase battlefield safety and to improve logistics and military prevention.

The third area where an unusually intensive concentration of research and developmental intellectual capacity and financial resources was realized was molecular biology, human genetics.The completion of the Human Genome Project itself gave a new impetus to the establishment of a new scientific field, namely *military genetics.*

However, at present scientific results that can potentially be used for military purposes can only be obtained diversely through research carried out in specialized laboratories. Reviewing the international publications on this topic I made the following observations:

1. There is a lack of unified, transparent framework and stratification of the military applications of genetics. The number of corresponding international publications highlights that a summary and analysis of our knowledge in the field of military science could provide new information for researchers and other experts.

2. When starting to organize the information I noticed that the known applications of military genetics focused on the description of objects, processes and personal identification. These genetic examinations and technologies may play an important part in improving combat preparedness, establishing an optimal deployment practice suiting the skills of the soldiers, improving logistics as well as improving disaster and military conflict management, the personal identification of the victims of accidents and mass accidents, the design of military secret service tasks, the fight against terrorism and the execution of military operative interventions.

3. My personal scientific field of interest started to take shape and narrow at the beginning of the 1990s with the Hungarian initiation of the basic research needed for the implementation of personal identification based on the human genetic material, the DNA. This research involved the examination of certain sequences or non-coding regions in the human genome (usually with tandem repeats) which – according to our present knowledge – do not carry information. Due to their diversity, these sequences proved to be suitable for the highly effective distinction and discrimination between persons.

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The development in the past decade allowed for the identification of coding, information carrier genes responsible for externally visible human characteristics (phenotype) including hair colour, eye colour, skin colour, age, height, baldness and certain diseases and as a result of modern genetic technologies predictive applications also became available.

The genetic determination of the colour of the human iris is one of these methods (DNA phenotyping), which can also be applied for military purposes. After getting acquainted with the eye colour prediction model submitted to the United States Patent and Trademark Office I saw ways for its further development and clarification since I realized that the model was only suitable for the prediction of blue and brown eye colours. Its predictive power for the third, so-called intermediate eye colour group (73%) is low therefore the colour composition of the iris constituting this group cannot be predicted reliably with this model. The structure of the model shows that it does not reckon with the green eye colour, which is in turn significantly represented in the Caucasian race (its incidence is about 5% in Hungarian samples), which may partially explain the low predictive power of the model for the colour group defined as intermediate. The procedure of determining the colour of the human iris, which serves as a basis for one of the statistical inputs for the model, is not standardized nor automated in the known publication because it was carried out under subjective circumstances placing human factors in the foreground. It is now clear that the gene loci potentially responsible for the genetic transmission of human eye colour have not been genetically tested oranalyzed.

RESEARCH OBJECTIVES

My research objectives were the followings:

- *To synthesize* the military applications of molecular genetics into a transparent framework. Military genetics involves the results of human and non-human basic and applied genetic research along well-defined directions, among which many were considered to be applicable only in the civil sector.

- *To highlight* the fact through the systematic review and meta-analysis of national and international publications that military genetic applications are and will be an organic part of military strategicplanning and that those applying the results of military genetics will have an indisputable advantage in the fields of logistics, reconnaissance, combat preparedness (human resource), self-defence, disaster management, effective reaction in the field of military secret service operative tasks and in almost all segments of warfare due to the ever expanding treasury of non-lethal weapons – respecting the frameworks of international law.

- After the classification I found it important *to point out* the connections of separate scientific subdivisions with special respect to the relations between military science and medicine, tactics and genetic research. I intended to describe the emergence and historical development of military genetic associations and relations over time and space through examples.

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- *To prove* that certain parts of DNA-based human phenotype prediction as a genetic application, especially the human eye colour prediction model, offer potential for military application.

- *To elaborate* an eye colour prediction model based on information technology and genetics which allows for the effective prediction of brown, blue, green and complex eye colours even in the case of an unknown individual leaving biological trace evidence and *to achieve*the objective determination of the character and ratio of individual colours constituting complex eye colours.

- *To create* a digitalized, pixel-based software system with low standard deviation and safely reproducible results based on iris analysis as a part of the prediction model, the operation of which and the character of the acquirable information does not depend on the subjective judgement of the examiner.

- Scientific publications suggest that several gene loci play a part in the transmission of the human eye colour. Another objective of the research was *to find* the lowest possible number of loci proven to play a part in eye colour transmission that is sufficient for eye colour prediction in the Hungarian population and the effective functioning of the computerized predictive model.

RESEARCH HYPOTHESES

1. The military application of human genetic research results is an inevitable part of future warfare. The review and analysis of the corresponding publications allow for the systematic classification of this separate field of knowledge and the description of developmental stages leading to the establishment of military genetics on the borders of traditional disciplines.

2. The review and analysis of international publications and the classification of the acquired information allow for the systematization of military applications in a way that the classification remains modifiable and extendable with the future development of research and applications.

3. Apart from DNA genotyping, the prediction of phenotype from biological samples is also an important part of military biometric personal identification.

4. A computer programme can be created for the establishment of the human eye colour prediction model which, using the low standard deviation of *HSV colour space Hue,* is suitable for the accurate, informative and pixel-based colour analysis of the human iris.

5. DNA-based human eye colour determination allows for the establishment of a prediction model which is able to predict the human green eye colour in contrast to the previously known prediction model which could only distinguish between blue and brown eye colours.

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6. Automated eye colour analysis allows for the prediction of colour compounds and their ratio in complex eye colours.

7. It is possible to statistically select the lowest possible number of loci playing a part in the transmission of human eye colour, which allows for the highest possible efficiency of the prediction model.

8. An eye colour prediction model can be created for the Hungarian population samplewith similar efficiency to that of the currently available models, which allows for the prediction of the eye colour of an unknown individual leaving biological trace evidence.

RESEARCH METHODS

As described in the chapter 'research hypotheses', the following methods were used to systematize military genetic knowledge:

- My primary aim was to study, research and analyze in detail the available, mainly international publications and systematize them according to their military applications. During this process I applied the methods of analysis, synthesis, induction, deduction and meta-analysis.
- I used the facts and summarized experience of scientific reactions and comments on my English and Hungarian presentations and publications from the previous years.
- I incorporated the recommendations of my consultant regarding the structure, layout, editing and prioritization of chapters as well as his critical comments after my presentation held on 27 October, 2011 at the 4th Doctoral Candidate Forum of Military Sciences for the Board of the Doctoral School of Military Sciences recommending the specification and prioritization of topics and the necessary incorporation of my own research results.

To establish a predictive eye colour model based on genetics and information technology:

- I reviewed and analyzed the published literature on the gene loci responsible for the transmission of human eye colour
- I collected biological samples from unrelated Hungarian individuals representing the Hungarian population
- In 2011 I joined the so-called Pigment Project led by Horolma Pamzsav M.D. at the DNA Laboratory of the Budapest Institute of Forensic Medicine belonging to the Institutes for Forensic Science and Research:
    - I performed so-called real-time Taqman® PCR tests to examine the genetic loci representing the human eye colour
    - I participated in the establishment of the IT software programme for the examination of the human iris colour, which incorporates the Gimp 2.8.0 programme and pixel-based modules integrating HSV colour space Hue.
    - I learnt to use the statistical databases and programmes R-project, MATLAB and MIDAS that can be used for creating the model.
    - I investigated the efficiency of predictive modelling with ROC analysis.
    - I performed comparative analyses of the efficiency of the eye colour prediction model based on the Hungarian population sample and that of the previously published eye colour prediction model.

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BRIEF DESCRIPTION OF THE RESEARCH IN CHAPTERS

I divided my thesis into three chapters in accordance with the research objectives stated above.

In the first chapter I gave a brief historical overview of the development of molecular genetics, then I discussed the different applications of military genetics in a summarized analysis in subsections based on the meta-analysis of the published literature: the genetic dimensions of military logistics and disaster management, the genetic applications for military purposes including the provision of the highest possible level of human military resource skills using genetic prediction and finally I analyzed the role of chemical materials in muta-, terato- and carcinogenesis.

In the second chapter I described the historical development of human personal identification based on DNA genotyping andthe structure of public civil and military DNA databases, I pointed out the robustness of examination methods through historical military examples and described the history, present structure and legal background of the Hungarian human DNA database.

In the third chapter I described the role of human DNA investigations in the determination of certain externally visible characteristics (age, hair colour, eye colour) and the process of personal identification using these examinations. I gave a detailed analysis of the examination of the structure (Daugman Iris Code®) and colour of the human iris and its present and future applicability in the process of biometric personal identification. I illustrated the process of DNA-based iris phenotyping using a new, pixel-based predictive model for human eye colour determination based on genetics and information technology. I defined the basis of the operation of the automated Pigment v.1.0 software system which is able to analyze the colour of the iris with a procedure using the low standard deviation of the HSV colour space Hue. I described the details of the establishment and statistical background of the eye colour prediction model and the stages and results of model retesting. I recorded the potential directions for its military application.

SUMMARIZED CONCLUSIONS

- The military application of human genetic research results is an inevitable part of present and future warfare. The analysis of corresponding scientific publications, synthesis, induction and deduction allow for the thematic systematization of this separate field of knowledge.

- The genetic and military developmental stages that led to the development of *military genetics* on the borders of traditional disciplines can be presented.

- The review and meta-analysis of international publications and the classification of the acquired data allow for the systematization of military genetic applications in a way that this classification can further be extended with the future development of research and applications.

- Apart from DNA genotyping, the prediction of human externally visible characteristics from biological samples is also an important part of biometric personal identification for military purposes.

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- A software system can be set up for the establishment of a human eye colour prediction model, which allows for the precise, informative and pixel-based colour analysis of the human iris using the low standard deviation of the HSV colour space Hue.

- DNA-based human eye colour determination allows for the establishment of a predictive model, which is suitable for the prediction of the human green eye colour in contrast to the previously known prediction model, which could only distinguish between the blue and brown basic eye colours.

- Automated eye colour analysis allows for the determination of individual colours and their ratio in complex eye colours.

- It is possible to statistically select the lowest possible number of genetic loci which is necessary for the highest possible efficiency of the prediction model.

- Biological samples of the Hungarian population allow for the establishment of a functioning eye colour prediction model, which can be used for the prediction of an unknown individual leaving biological trace with similar efficiency to the currently available models.

- Apart from financial difficulties, the legal and social acceptance of the entire potential of military genetics is doubtful. Based on religious, moral or ethical reasons, several people and countries have objections against any endeavour to change and/or use the genetic material of plants, animals and humans. *The prohibition of genetic discrimination and offensive military use* recorded directly or indirectly in the constitutions of the countries (laws and other legislations) andinternational conventions serve as a firm basis for the argument system of civil organizations and defenders.

- On the other hand, countries and groups with less strict legislative conditions regarding genetics may have an advantage in the field of genetic revolution by allowing the application and testing of basic biogenetic research results both in the civil and military sectors.

- The 21st century results of biotechnology and the completion of the HGP served as a basis for the development of a new field of science, namely *military genetics*. Military genetics involves the results of human and non-human basic and applied biotechnological and genetic results along well-defined directions, among which some were previously considered to be applicable only in the civil sector.

- The currently available and future applications will be organic parts of military strategic planning and those applying the results of military biogenetic research will have an indisputable advantage in the field of reconnaissance, combat preparedness (human resource), self-defence, disaster management and effective reaction as well as in nearly all segments of warfare due to the ever increasing treasury of non-lethal weapons – respecting the frameworks of international law.

- The increasing number of potential military applications may have another consequence for those choosing the army as a career. *In the future, the right of disposal with the information recorded in our own genetic material, which is essentially linked to self-determination, may be offended at the moment of entry into military service.*

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- The issues mentioned above highlight the close relationship between military bioethics and military genetics and the need for spreading genetic knowledge in current gradual and post-gradual education as well as at the level of political and military decision making.

NEW SCIENTIFIC RESULTS

- I defined the concept of 'military genetics' as a borderland study. Military genetics refers to the military application of human and non-human molecular biological and genetic research results. I created a transparent and upgradable system of this knowledge, into which new military genetic information can be integrated with the future development and change of science.

- I designed a software system for the automated colour analysis of the human iris colour (Pigment v1.0), which is based on the low standard deviation of the HSV colour space Hue.

- I established a macro model capable of the prediction ofthe human iris colour integrating the Pigment v.1.0 software system, which allows for the prediction of the human eye colour, one of the phenotypic characteristics determined by the human DNA, from biological samples with appropriate statistical value.

- I proved that this software programme was suitable for eye colour prediction in samples of people born in Hungary with similar statistical value to that of previous models applied for other populations. Furthermore, I proved that the model could be used to predict the green eye colour, which is relatively common in the Hungarian population.

- I proved that it was possible to create an eye colour prediction modelcapable of determining four eye colour groups with appropriate statistical accuracy based on DNA examinations, which colours are easily distinguishable even for the outside observer.

- I proved that the most informative examination for genetic eye colour determination and prediction was SNP testing on chromosome 6 even in samples from the Hungarian population and that its efficiency cannot be further improved by increasing or decreasing the number of SNP loci constituting the set.

RECOMMENDATIONS

In the present thesis I provided a cross-sectional snapshot in the field of military genetics pointing out wider aspects of the topic and already realized applications. I presented the potential targeted military applications for automated genetic eye colour prediction as an informative supplementary marker test.

Due to the incredibly dynamic improvement of military genetic knowledge (and its simultaneous rapid depreciation) it is necessary to extend the knowledge of every citizen in this field and it should be a part of responsible social, political and military thinking.

This is essential for making informed decisions about the usefulness, conviction or refusal of the civil and particularly military application of biotechnological and genetic methods.

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Hungarian military science has started to involve military biogenetic knowledge, certain elements of which – in the chapters summarizing mass destruction and non-lethal weapons – can already be found. The continuous and rapid development of genomics (and biotechnology) obviously leads to the realization that 'the next most logical move of modern warfare is to turn to military biogenetics'.

However, little is known about the attitude of the audience towards the biogenetic revolution which is just about to happen in military science and about the adaptation power of gradual and post-gradual students (future decision-makers), teachers or present decision makers regarding the application of military genetic results.

Future military strategic planning or the establishment of national security concepts, the selection of research-developmental project priorities and the distribution of the available financial resources are not possible without this knowledge. Therefore I recommend the consideration of the thoughts and conclusions of my thesis to decision makers.

Due to the upgradability of the elements of this thesis and the possibility of adding up-to-date knowledge I find it suitable for the development of educational materials in gradual and post-gradual education, further training and other courses.

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THE DOCTORAL CANDIDATE'S LIST OF RELEVANT PUBLICATIONS

(17 June, 2014): Impact Factor: 12.213, total citation: 42, independent: 26

English and Hungarian reviewed publications

1. **Kozma Zs.**, Sétáló J., Bajnóczky I., Yamada M., Yamamoto Y., Nishimura A., Ushiyama I., Nishi K.: Genetic Study in a Hungarian and in a Japanese Population at the Short Tandem Repeat Locus HUMVWFA31. **Journal of Shiga University of Medical Science, 12(1997) 51-59.**

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9. **Kozma Zs**., Huszár A.: A katonai biogenetika: a biotechnológia és a molekuláris genetika eredményeinek katonai alkalmazásai **Hadmérnök, VI. 4 (2011) 94-110.**

10. **Kozma Zs.,** Sandor G., Pamjav H., Huszar A.: The human iris polymorphisms: computer-based and genetic assessments of human iris and possible applications in human identification**AARMS 2:12 (2013) 229-247.**

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1. **Zsolt Kozma,** Gábor Sándor, Horolma Pamjav: Predicting of human eye color as an external visible characteristic (EVC) using informative SNPs and its possible applications: preliminary results, 5th International Symposium of the Osteuropaverein On Legal Medicine 12-14 April 2012, Regional Centre of the Hungarian Academy of Sciences, Szeged, Hungary

2. **Kozma Zs.,** Yamada M., Nishi K.: A Novel Approach for Genotyping of the ABO Blood Group System. (presentation) 6th Alpok-Adria-Pannónia Scientific Meeting of Forensic Medicine, 5-7 June 1997, Veszprém

3. **Kozma Zs.,** Szántó L., (2002) Genetic testing in adoption. 11th International Meeting on Forensic Medicine Alpok-Adria, 2-5 May 2002, Visegrád

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1. **Kozma Zs.** and Wiegand P. (1994) Investigations of the STR systems HumACTBP2 (SE33), HumTH01 (TC 11) and HumVWA (vWA) in Hungarian population 73th Annual Meeting of the German Society of Legal Medicine, Münnich, Germany, 1994 Z. Rechtsmedizin. 42:6 (1994) 423.

2. **Kozma Zs.**, Bajnóczky I., Usiyama I., Nishi K.: Allele Frequency Distribution of the STR Systems HumTH01, HumTPOX and HumCSF1PO in Two Racial Groups: Hungarian and Japanese Population Data. (1996) ISFH (International Society of Forensic Haemogenetics) Hakone Symposium on DNA Polymorhisms, Hakone, Japan, August 22-24, 1996 (Book of Abstracts p41, No.:P10)

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