

# Illegal Kidney Transplantation: The Utility of Genetics in the Fight Against Trafficking of Human Being

## Abstract

In the last decades organ transplantation has become a standard and successful medical procedure. Increasing requests and improved medical and technical skills are in contrast with the global lack of organs. The imbalance between supply and demand of organs has created a profitable black market that promotes illicit organ trafficking, with a big loss of human lives.

Actually, forensic genetics allows the use of tools capable of bringing this trade to light. For patients whose clinical history is unclear, it is relatively easy and inexpensive, during the post-operative period, genetically typing an urine sample comparing it to the database of missing people in order to verify if the transplanted organ can be ascribable to a missing person. We postulate to use ancestry-informative genetic marker analysis as a useful tool to identify the geographical origin of transplanted organ and to contribute to the fight against illegal kidney trafficking.

This practice produces important ethical issues: in Italy, according to Article 365 of the Criminal Code, there is an obligation to report for physicians who have worked in cases that integrate offences prosecuted ex officio. This rule does not apply when the patient could be exposed to criminal prosecution. The Italian law 675/1996 provide specific rules for sensitive data, which include genetic data. Thus, the genetic analysis of urine samples can be problematic. A possible solution could be make anonymous samples prior to the genetic investigation, with the exclusive purpose of verifying whether the transplanted organ is from a missing person.

**Keywords:** Kidney; Transplantation; Genetics; Trafficking; Black market; Single nucleotide Polymorphisms; Missing person DNA database

**Abbreviations:** STRs: Short Tandem Repeats; SNP: Single Nucleotide Polymorphism; HGDP: Human Genome Diversity Panel; HESC: Human Embryonic Stem Cell; SCNT: Somatic Cell Nuclear Transfer

## Introduction

The first successful kidney transplant was performed at the Brigham Hospital in Boston in 1954 [1]. Ever since, organ transplantation has developed into a well-established medical practice which improves the quality of life of thousands of patients every year, and it has become a standard and successful medical procedure. The Guidelines on kidney transplant of the European Renal Association claim that “all patients with end-stage disease should be considered for renal transplantation unless they have absolute contra-indications, because renal transplant offers a better life expectancy and quality of life than dialysis”. For these reasons, kidney transplantation is now considered to have a more favorable cost benefit than dialysis therapy [2].

Organ transplantation is anonymous, completely free of charge and, in most countries, it is regulated by national laws. In Italy the deceased-donor (formerly known as cadaveric) transplantation is the most important type of transplantation. In this context, in many poor countries a black market of organs is flourishing. Black market happens when the demand for goods exceeds the supply,

as it occurs with organs for transplantations. Organ trafficking provides an attractive and lucrative area for criminal groups because of the high demand and low supply. Ethical reasons require solutions to curb this crime.

## Kidney Transplantation

Kidney transplantation is the transplant of a kidney into a patient with end-stage renal failure. Normally, depending on the source of the donor organ, kidney transplantation is classified as deceased-donor or living-donor transplantation. Deceased-donor transplantation is the transplantation from a deceased individual, conversely, living-donor renal transplants are surgeries further characterized as genetically related (living-related) if a biological relationship exists between the donor and recipient or non-related (living-unrelated) transplants.

End-stage renal failure, regardless of the primary cause, is the indication for kidney transplantation.

After surgeries immunosuppressant drugs are used to stop the immune system from rejecting the donor kidney. The most common therapy is a cocktail of tacrolimus, mycophenolate, and prednisone. Since drug therapies to prevent rejection are so effective, donors do not need to be genetically similar to their recipient, increasing the utilization of living donors. The

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**Eugenia Carnevali<sup>1\*</sup>, Gabriele Margiotta<sup>2</sup>,  
Federica Tommolini<sup>1</sup>, Susanna Massetti<sup>1</sup>,  
Giorgia Tasselli<sup>1</sup> and Simona Severini<sup>1</sup>**

<sup>1</sup>Section of Legal Medicine, University of Perugia, Italy

<sup>2</sup>Section of Legal Medicine, University of Siena, Italy

**\*Corresponding author:** Eugenia Carnevali, Università degli Studi di Perugia, Sezione di Medicina Legale–Piazza Lucio Severi 1, Perugia, Umbria, Italy, Tel: +390744205055; Fax: +390744220236; Email: eugeniacarnevali@gmail.com

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prognosis after kidney transplantation is generally excellent, with 1-year graft survival rates ranging from 80% to 95%. After kidney transplantation, the patient must be periodically tested by physicians.

### **Donation from Living Donors**

Due to the scarcity of deceased kidney donation (in some countries this donation does not exist or is not encouraged), and since anti-drug rejection therapies are so effective (whereby donors do not need to be genetically similar to their recipient), in many countries, living kidney donation has become the most important alternative to meet the increasing amount of patients in need of transplantation. For this reason, in the United States, the use of living donors is rising. In 2006, 47% of donated kidneys were from living donors [3].

### **The emerging problem of illegal traffic of organs and transplant tourism**

Increasing demands of kidney transplantation and improved medical and technical abilities are in contrast with the global lack of organs. The imbalance between supply and demand of body parts has created the basis for a highly profitable black market in organs that gives rise to criminal activities, inserting it in the broader context of the trafficking of human beings [4].

The definition of trafficking of human beings is in the "Protocol to Prevent, Suppress and Punish Trafficking in Persons, Especially Women and Children supplementing the United Nations Convention against Transnational Organized Crime" (the so-called Palermo Protocol) published in 2000: "the recruitment, transportation, transfer, harboring or receipt of persons, by means of the threat or use of force or other forms of coercion, of abduction, of fraud, of deception, of the abuse of power or of a position of vulnerability or of the giving or receiving of payments or benefits to achieve the consent of a person having control over another person, for the purpose of exploitation. Exploitation shall include, at a minimum, the exploitation of the prostitution of others or other forms of sexual exploitation, forced labour or services, slavery or practices similar to slavery, servitude or the removal of organs" [5].

The trafficking of organs may appear to be limited, as it accounts for less than 0.2 per cent of the total number of detected victims of trafficking in persons. Nonetheless, cases of such traffic were officially reported in 16 countries and it appears that all regions are affected, this suggests that the phenomenon is not as marginal as the number of victims officially detected suggests. In 2006 Michele Goodwin, an associate Law Professor and Director of the US Health Law Institute, introduces the term "transplant tourism" or "organ tourism", describing it as "black market shopping in the new lexicon of organ transplantation", and he inserted it in the "travel for transplantation" that is the movement of organs, donors, recipients, or transplant professionals across jurisdictional borders for transplantation purposes.

Transplant commercialism is the practice in which an organ is treated as a commodity, being bought or sold or used for material gain. Organs are sold by individuals resident in poor countries and purchased by wealthy individuals residing in affluent economies.

The main countries of origin of the "sellers" are traditionally China, Pakistan, Egypt, India, the Philippines, Colombia. Recently Kosovo, South Africa, and Brazil and other Latin American countries have been added to the list. Buyers, for the most part, originate in the United States, the Gulf Countries, Israel, Japan, Australia and Canada.

### **Missing person DNA data-base to combat the illegal traffic of organs**

At present, the high level of data quality reached by the analytical techniques used in forensic genetics allows the use of tools capable of bringing to light the trade of organs. The biological basis of this statement is that urine of a transplant recipient contains cells from both the donor and the recipient because of the mixture of cells deriving from the transplanted kidney and the lower urinary tract of the recipient. The genetic profile of the recipient can be obtained by analyzing an oral swab, while the genetic profile of the donor could be obtained by subtraction. So, it is relatively easy and inexpensive genetically typing a sample of urine during the post-operative renal transplantation follow up from patients, of which the clinical history is not known with accuracy. The genetic data can be compared with the database of missing persons (where it is available) in order to verify whether the transplanted organ can be preferable to a missing person.

In forensic genetics the method of choice for personal identification is typing of Short Tandem Repeats (STRs) loci due to their high power of discrimination and to the availability of allele frequency data for a large variety of populations. In the last years different forensic applications have come into focus. At present Single Nucleotide Polymorphisms (SNPs) typing have proved their worth in important supplementary information such as identification of severely degraded DNA in skeletal remains, complex relationship tests, physical appearance of DNA donors and prediction of biogeographic ancestry of an unknown stain donor. For this application, in fact, STRs are less useful due to their mutational instability and resulting high intra-population variability compared to relatively low inter-population variability [6]. The SNP genotyping of the CEPH Human Genome Diversity Panel (HGDP-CEPH) is a project started by Stanford University's Morrison Institute with the collaboration of scientists around the world. The scientific community has used the HGDP data to study: human migration; mutation rates; relationships between different populations and genes undergoing selection. Stanford's HGDP-CEPH studies have been instrumental for the assessment of human diversity, providing information about similarities and differences in human populations. Through this project, many studies have been carried out with the aim to identify panels of markers suitable for the identification of the geographical origin of a subject. The analytical tools that appear most suitable for this purpose are SNPs (Single Nucleotide Polymorphisms) [7].

Because of this recent availability of genetic data concerning many populations of the world and the concomitant development of technologies and methodologies that are appropriate to the study of panels of SNPs, it's possible to establish genetic tests capable of differentiating the geographic origin of the two cell populations detectable in the urine of persons who have received a kidney transplant. We postulate that it is possible to use ancestry-

informative genetic marker analysis as a scientific tool to identify the geographical origin of transplanted organ and in this way to contribute to the fight against the illegal traffic in human kidneys. After adequate studies, in future it will be possible to discover “irregular” transplants and to bring appropriate actions against the illegal traffic of organs [8].

## Conclusion

The global shortage of organs for transplantation and the actual impossibility of building artificial organs are the principal causes of the illegal traffic of organs. At present a possible solution for solving shortage of organ donor could be represented by tissue engineering. Recently some encouraging results have been achieved. Next-generation regenerative medicine will open a new avenue for manipulation of epithelial-mesenchymal interactions to guide organogenesis. In the future it will be possible the synthesis of new types of miniorgans [9].

Research on embryonic stem cells offer hope for new therapies, but raises an ethical issue. It forces us to choose between two moral principles: the need to prevent or alleviate the suffering, and the need to respect the value of human life. The moral status of the embryo is a complex and controversial issue. Religions have different considerations of the status of a human embryo at an early stage. For example, the Catholics, Orthodox and Protestant conservatives believe that the embryo has the status of human being from the moment of conception and do not allow any kind of embryo research. Judaism and Islam emphasize the importance of helping others and believe that the embryo does not reach the full status of a human being before 40 days, thus allowing some research on embryos.

Recently, for the first time, a group of scientists has successfully produced human embryonic stem cells (HESCs) using the technique of nuclear transfer [10]. The somatic cell nuclear transfer (SCNT) is a technique in which the nucleus of a donor cell is transferred into an egg cell whose nucleus has been previously removed, generating embryonic cells genetically identical to the donor to the exclusion of the mitochondrial DNA. The nuclear transfer is proposed as a technique for the production of stem cells specific for a patient, which are generated directly from the somatic cells of the same patient with the addition of a cocktail of cellular factors capable of stimulating the regression of somatic cells to a stem cell state [11].

Another solution to increase the supply of kidneys for transplants proposed by some physicians is a regulated kidney donation system with economic benefits. This system, however, can be irregular in many Nations. In Italy, for example, regulated kidney sales is impossible because 5th Art. of the Italian Civil Code states “The disposal of the body is prohibited when it cause a permanent diminution of physical integrity or is otherwise contrary to law, public order or morality”. Each country should implement programs to prevent organ failure and to provide organs to meet the transplant needs of its residents from donors within its own population. Efforts are essential to enhance deceased donor transplantation through educational programs.

We postulate the possibility of genetic characterization of the urine samples of the patients whose the clinical history isn't clear.

This type of investigation opens important bioethical scenarios. For example, in Italy, it is an obligation to report (Art. 365 of the Penal Code) for physicians who have worked in case that include offences prosecuted ex officio. This rule does not apply when the report of this activity could expose the patient to criminal prosecution. In addition, the Italian law n.675/1996 and other legislative decrees, regulations and codes that have taken place in recent years provide specific rules for sensitive data, which also include health and genetic data. Thus, the genetic analysis of the urine sample of a transplanted subject with unknown clinical history becomes problematic.

The main ethical assessment to be made regarding the possibility of identifying the illicit trafficking of organs by using urine samples collected during post-operative follow-up is the lack of consent to carry out surveys other than those designed to monitor the correct functionality of the transplanted organ. Any medical investigation, and genetics one in particular, must be authorized by the patient who must provide a written consent after being fully informed of the purposes and methods of the survey. In addition, the physician is obliged to ensure that the patient has correctly understood the given information [12].

The genetic analysis could be characterized essentially in two phases: the first stage involves the genetic analysis of urine samples through markers for the identification of the likely geographical origin of the donor graft. Once identifying geographical region of the donor, the second phase could be the comparison of the donor genetic profile with the data-base of the missing person of the involved Nation. The proposal of analyzing anonymous urine samples avoids any conflict arising from consent to the execution of the survey and, at the same time, it allows monitoring of the criminal phenomenon which is an essential prerequisite for any attempt to restrict or combat illicit trafficking of organs.

The comparison with published data related to genetic markers for identifying the geographical origin and the comparison with the data-base of the missing person do not involve ethical problems because, in the first case, allele frequencies are related to anonymous data, and, in the second case, the consents were acquired at the time of the introduction of the sample in the database. It is useful at this point to reiterate that the missing person data-base are materially different from the genetic data base established with forensic purposes. The establishment of the latter has been proposed and implemented in many countries to provide a valuable element in the resolution and prevention of crimes. In conclusions, National and International Laws are necessary to establish a redundant, feedback control system not only at the transplant stage, but also during the follow-up, particularly in cases of patients without a clear clinical history.

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