Background Paper for the International Conference

Policies, Regulations, and Bioethics of Genomic Research

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Qatar Genome Programme (QGP) & Research Center for Islamic Legislation and Ethics (CILE)

In the wake of the successful completion of the Human Genome Project (HGP) by the beginning of the twenty-first century, various countries worldwide started creating their own national genome programs following, in broad lines, the HGP model. The Gulf region was no exception in this regard. In December 2013, the Qatar Genome Programme (QGP), was launched with the aim of charting "a road map for future treatment through personalized medicine". In the same month and same year, the Saudi Human Genome Project also took off. Besides these two leading projects, other initiatives have already started or are under development in other Gulf countries like Kuwait, Oman, Bahrain and the United Arab Emirates where the Ministry of Health and Prevention has recently unveiled the UAE Human Genome Project in 2017.

These initiatives make part of these countries' long-term plans to invest in knowledge-based economies because genomic research seems to be a wise future investment. Of the 7,000 inherited rare diseases identified worldwide, only 5% have treatments currently. Rare inherited monogenic diseases represent a significant burden in the Gulf region and particularly in Qatar. That is why the abovementioned initiatives and the resulting progress have been motivated by health- and economy-related interests and prospective benefits, e.g., the potential to prevent or treat some of the genetic conditions prevalent in the Gulf region, which usually put huge financial burdens on these countries' national budgets.

Besides the promising benefits and the great potential of genomic research and its applications, some of the most daunting challenges were and remain to be the ethical questions and dilemmas generated by the developments in this field. That is why the celebrated HGP dedicated substantial amounts of money (more than $14 Million annually) from its budget to examining the ethical aspects of the project through the Ethical, Legal and Social

Implications (ELSI) program. Subsequently, almost all national genome initiatives developed their own ELSI-like program bearing in mind the well-established fact that the information gained from mapping and sequencing the human genome will have profound implications for society. As far as Gulf countries are concerned, the Islamic religio-ethical tradition makes integral part of the moral landscape of these societies. That is why the ELSI work made by the national genome initiatives in countries like Qatar and Saudi Arabi pay special attention to Islamic ethics besides studying relevant international bioethical deliberations.

The forthcoming conference "Policies, Regulations, and Bioethics of Genomic Research" is a prototypical combination of international bioethical deliberations and the Islamic ethical perspectives. This call for papers exclusively concerns the second aspect, namely Islamic ethical perspectives, which will address topics with relevance to three main themes as outlined below.

Main Themes and Key Questions

Prospective papers are to address issues related to one of three broad themes, viz. (1) genetic counseling, (2) return of results and the ethical management of incidental findings and (3) genomic data ownership and sharing. Below, we give an overall explanation of each theme and its associated ethical questions espoused with tentative suggestions of how these questions can be addressed from an Islamic ethical perspective.

(1) Genetic Counseling

The genomic revolution has produced massive amounts of information related to our genetic makeup and how it can affect our current and future health condition. These massive amounts of information are extremely diverse and of varying degrees of certainty/probability. That is why their possible implications and consequences on one's life or that of his/her future offspring and broad family members are not easy to estimate and calculate. That is why "genetic counseling" was introduced as a professional process in which trained and expert counselors would help patients and their families take informed decisions.

In genetic counseling, the counselors' knowledge about genetics is as important as their knowledge about the counselees' cultural norms and religious beliefs because both aspects would determine which options are

more suitable than others for specific individuals in specific situations. Thus, genetic counselors who deal with Muslims need to be equipped with basic knowledge of the broad spectrum of ethical positions within the Islamic tradition so that they can give cultural- and religious-sensitive advice in significant life events or crises experienced by their clients. Below, we give a number of typical cases and questions which genetic counselors usually encounter.

(A) Reproductive setting

Discussing possible genetic risks within the reproductive setting is one of the most common issues in genetic counseling to the extent that one can speak of a distinct sub-category called "reproductive genetic counseling". A long list of ethical questions and dilemmas falls within this sub-category and guidance from the Islamic perspective will be of help for both the counselors and their Muslim counselees. It starts before marriage when the to-be-married couple, especially when they come from families known for history of genetic conditions, undergo the so-called pre-marital genetic test. The ethical dilemma shows up when the results of the test demonstrate that the future couple, although they have no symptomatic diseases, carry genetic mutations which may cause genetic abnormalities for their future offspring. The possibility that these two persons will have such children is usually a matter of high/low probability with percentages that can reach up to 25% in autosomal recessive diseases or even 50% in autosomal dominant ones, and can be sometimes higher or lower, depending on the inheritance pattern of the disease and genetic makeup of the to-be-married couple. By having such results, the future couple can choose not to marry but they can still get married and then look for other options like not having children at all or trying to procure children without genetic abnormalities. For instance, they can use Assisted Reproductive Technologies (ARTs) through which fertilized eggs can be genetically tested and only those without genetic abnormalities will be implanted into the wife's uterus, the so-called Preimplantation Genetic Diagnosis (PGD). If natural pregnancy happens, the couples can still do genetic tests during pregnancy and based on the results of genetic tests, they can decide if they want to continue or terminate pregnancy, the so-called Prenatal Diagnosis (PND).

Throughout all these possible steps, both genetic counselors and counselees are in need of overall knowledge about what is ethically acceptable or

unacceptable within the Islamic tradition and on what basis they can judge the optimal course of action. Examples of the questions they face include the following: Would the information revealed by the pre-marital genetic test make a sufficient ground for declaring marriage between such couples as reprehensible or maybe even forbidden because of the genetic risks, which threaten their future offspring? Some studies show a correlation (however, not always a cause-effect relationship) between consanguineous marriage and having children with genetic mutations. Would this risk affect the religious ruling of consanguineous marriage in particular? If only one of the partners came to know about his/her genetic risks, should he/she inform the other partner before marriage? If the couple decided to get married anyhow, are they under obligation to undergo the aforementioned genetic tests before or during pregnancy and choose the embryos who have no genetic complications? What if the married couple disagreed on what to do with their embryos before or after pregnancy, whose opinion should prevail? What if the rest of the family was supportive to one of the future parents, would this factor be relevant for the decision-making process? Finally, what information should the counselor provide for his Muslim counselees who feel lowered self-esteem, guilt, shame, or blame because of having a child with a genetic condition? How should the counselor deal with the couples who believe that they have such a child because of an evil eye rather than anything else?

(B) Common disease setting

Besides the reproductive setting, genetic counseling also deals with the so-called common disease setting, including cancer-, cardiovascular-, and neuro-genetics. The main audience that genetic counselors deal with in this context are patients, usually adults with family history of genetic conditions, who seek to understand their own risk and susceptibility for disease and to estimate the likelihood of a late onset genetic condition. This means that the genetic tests conducted in such cases fall under the category of "predictive medicine" rather than the usual "therapeutic medicine". One of the famous examples in this regard is the genetic test conducted for detecting mutations in BRCA1/2 genes associated with familial forms of breast cancer.

Unlike other genetic tests, whose results could convey a higher level of probability and even sometimes certainty, the BRCA1/2 tests usually do not predict with certainty (probability increases by about 40%) that a certain woman would get breast cancer in the future. Recent estimates show that

about 12% of women in the general population will develop breast cancer sometime during their lives. However, 55% to 65% of women who inherited a harmful BRCA1 mutation and about 45% of women with the BRCA2 mutation will develop breast cancer by age 70 years, and according to some studies this percentage can even go up to 80% or more. This means that still some women with BRCA1/2 mutation may never develop cancer and they may die because of other non-cancer related conditions. The results of these genetic tests, however, give the clients more options instead of just waiting for the possible onset of a lethal disease and going through the suffering process, which they may have experienced with other cancer patients in their family, like one's mother or grandmother. There is the option of conducting increased surveillance through more frequent breast cancer screening (enhanced screening) so that breast cancer can be detected at an early stage. Women found to be BRCA1/2 carriers can also opt for the cancer risk-reducing surgery of prophylactic mastectomy. This was the option used by the famous Hollywood actress Angelina Jolie whose mother and maternal grandmother died of cancer. When she did a genetic test and the results showed that she carries a cancer-causing mutation, Angelina decided to have a double mastectomy in 2013 and she spoke about her case openly. Recent studies speak of "Angelina Jolie effect" in the sense that her story did encourage more women to get themselves tested for breast cancer.

It is to be noted that the risk-reducing surgery of prophylactic mastectomy does not guarantee full protection against cancer. Academic studies showed the possibility of cancer recurrence for women who have undergone the surgery. Besides this major risk, this irreversible surgery also entails a number of other possible harms, e.g. affecting woman's psychological well-being due to a change in body image and the irreversible loss of normal breast functions, causing a sudden drop in estrogen production, which will induce early menopause in a premenopausal woman. This early menopause can cause an abrupt onset of menopausal symptoms, including hot flashes, insomnia, anxiety, and depression, and some of these symptoms can be severe. This early menopause may also include some long-term effects like the decreased sex drive, vaginal dryness, and decreased bone density.

In the midst of this jungle of probabilities, percentages, and various options, which always entail both benefits and harms, genetic counselors are in need of general rules and governing maxims. The prospective papers are expected to outline the relevant rules and maxims and to show how they can be

applied to the abovementioned ethically challenging scenarios and examples and help counselors and counselees deal with questions like: should women undergo such genetic testing? If the results showed their susceptibility to diseases like cancer, which options are (in)compatible with Islamic values? How can they prioritize these options?

(C) Children

All the abovementioned scenarios were presented in the context of an adult person (*baligh*). However, in many of these cases the involved person can be a minor (*saghir*) as well. Ideally, the genetic counselor would consult the child's parents and discuss possible options with them both. But if parents disagreed on the best course of action for their child, whose opinion should prevail, under what circumstances and why? Additionally, if both parents cannot give their consent, for one reason or another, who should be entitled to decide for the child? On the other hand, should the opinion of the child be considered in certain cases, whether his/her opinion would be in line with the opinion of one of the parents or against the option endorsed by both of them? Would the discerning (*mumayyiz*) versus non-discerning (*ghayr mumayyiz*) categorization make any difference in this regard? It is to be noted that genetic testing can predict certain inherited conditions many years before their onset. That is why some tests are developed, as a predictive procedure, to examine the possibility of a late onset of a genetic condition. This means that the test can be done while the tested person is still minor, but the genetic condition will not manifest before reaching majority (*bulugh*). Would the opinion of the child measure much heavier in this case than in other situations? Would it be better to postpone the genetic test until the child becomes adult, even if this delay may entail some (minor) risks? What if both parents or one of them insisted that their child undergo predictive genetic testing for adult-onset conditions? Although there may be no medical necessity at the moment for doing such genetic testing, parent's intention here is to achieve their children's best interest, especially when they are concerned about a genetic condition which is common in their family. Usually the core ethical issue is whether the involved person should be approached as 'current child' or as 'future adult' and also whether parental anxiety about their child's future genetic status should be part of balancing possible harms and benefits of such testing. Finally, would it make difference, from an ethical perspective, if the genetic testing has to do with

(autosomal recessive) carrier status or with developing, or being at risk of, a serious medical condition like Huntington or cancer?

(D) Nondirectiveness

Nondirectiveness has been for decades one of the core values of genetic counseling in international ethical deliberations, but many of its aspects remain debatable and sometimes even controversial. The mainstream understanding of nondirectiveness is that the genetic counselor should provide neutral, balanced and value-free information and stay aloof from decisions, which should be taken by the counselee alone. This is because, the advocates of nondirectiveness argue, the counselor has not experienced the emotional impact of the counselees' problem, nor is he/she intimately acquainted with their environment.

How should nondirectiveness in the context of genetic counseling be approached from an Islamic ethical perspective? Is it an absolute and unconditional value that the genetic counselor should always stick to and would only depart from in exceptional cases? If yes, what are the criteria, which makes a case exceptional?

(2) Return of results and the ethical management of incidental findings

To have a rough idea about the volume of possible results which one can get from reading and sequencing the genome, we present a concise overview of the human genome and how big it is. Scientists estimate that our human body contains about 37.2 trillion cells. With few exceptions, each of these trillions of cells contain a genome. The genome consists of the complete set of our deoxyribonucleic acid (DNA), a chemical compound that contains the genetic instructions needed to develop and direct the activities of every organism. DNA molecules are made of paired strands where each strand is made of four chemical units, called nucleotide bases or simply the letters A, T, C and G. The human genome contains approximately 3 billion of these base pairs or letters, which reside in the 23 pairs of chromosomes within the nucleus of all our cells. Scientists and ethicists usually use the "book of life" metaphor to describe the magnificence and magnitude of the human genome. If this book composed of 3 billion-letters is printed in regular font size on normal bond paper, the printed material will be as high as Washington Monument (555 feet high, about 169 meters, which is just over

fifty stories). A live reading of this text at a rate of one letter per second would take thirty-one years, even if reading continued day and night.

This magnificent volume of the human genome is quite telling about the immense amount of information that can be extracted from. Reading and sequencing the genome or exome, whether for clinical or research purposes, are usually meant for tracing specific pieces of information like discovering the genetic etiology of certain diseases among certain individuals or groups of people. However, researchers and clinicians understand that it is very likely that they will come across results which were not part of the original purpose of the research project or clinical test, the so-called "incidental findings". Because of the frequent occurrence of these incidental findings in the field of genomics and their complex nature, increasing discussions are now focusing on how these incidental findings should be managed from an ethical perspective. One of the key problems of the ethical management of incidental findings is that they are greatly diverse. Some of these findings are medical in nature, i.e. related to the health condition. Within this category, some of the findings have clear clinical utility in the sense that they reveal, with a high degree of probability, the individual's susceptibility to a disease and measures can be taken to protect the concerned individual from this disease. Other findings in this category can reveal one's susceptibility to a disease but the disease is untreatable at the moment and a third type of the findings within this category may not reveal anything that can be interpreted today, but its exact medical implications may be understood in the future. A substantial part of the incidental findings falls within the category of non-medical findings, such as the (misattributed) paternity and ancestry.

Against this background, both researchers and clinicians who come across such findings and also policy makers face questions like: Which incidental findings should be communicated to the research participants or patients? To whom these findings should be communicated (to the involved person only, to family members who may also be at risk, or maybe to governmental authorities)? What should be done in case the incidental findings have to do with a minor child and the findings relate to an adult-onset condition? How should the incidental findings be managed if they relate to a person who already died? Should we make a distinction, from an ethical perspective, between the context of research and that of clinical testing? For more information about this theme, the prospective authors can consult the recently published study *Genomics in the Gulf Region and Islamic Ethics: Ethical*

Management of Incidental Findings, by the World Innovative Summit for Health (WISH) in Doha, Qatar. The full text of the study can be accessed via this link https://www.imperial.ac.uk/media/imperial-college/institute-of-global-health-innovation/Islamic-Ethics-Report-English-(1).pdf

(3) *Biological specimen samples and genomic data ownership*

Scientific research conducted by national genome projects worldwide, including the aforementioned ones in Qatar and Saudi Arabia, is depending on having biological specimen (e.g. blood, saliva, tissue, and tumor) donated by individuals. Recently, there is also interest in conducting research on microbiomes by collecting microbial samples, which people generally used to consider them waste (e.g. dead skin, feces and some biobanks now also use poop). Each sample of these biospecimen 'belongs' to the individual it came from, in one way or another, at least for a defined period of time. That is why there is now a solid consensus among the ethicists that obtaining informed consent from the individual who donates the sample is mandatory. Without a proper informed consent, scientific research conducted on such samples is considered unethical. There is, however, much controversy about how far a potential research participant can truly give informed consent for a research project in which potential outcomes and effects are unknown, and when the very nature of future research to be conducted may not yet be conceived yet. As possible solutions, some ethicists proposed obtaining broad consent from the beginning or re-consenting the individuals who donated the samples on a regular basis. Available bioethical deliberations within the Islamic tradition hardly touch upon the informed consent and these related issues and do not explain what the acceptable position would be from an Islamic ethical perspective.

The other side of the picture is that scientists work on the samples donated by the individuals and conduct rigorous research on them so that they can eventually get data. These data can be published in academic journals and can also contribute to technology development (like drug or software), which may eventually lead to economic gain through intellectual property, sales and marketing, patenting and so on. These resulting data 'belong' to the scientists who conducted the research and that is why their names appear on the published work. The names of the research participants, to whom the donated biosample 'belong', do not appear on the published data.

Besides the research participants and the scientific researchers, there are also other important stakeholders including the biobank, funding agencies and the institution housing the biosamples.

Against this backdrop, the issue of ownership remains one of the key and complex questions in this field; who owns the biological sample and the resulting data and can the two (samples and the data) be separated from each other in this regard? In international bioethical literature, we have two opposing views. Some ethicists and lawyers defend an absolute non-patrimonial view of the human biosample, which means that there is no property right. This view is shaped by the fundamental principle of the prohibition against financial gain from the human body and its products, and also by the philanthropic idea that the donation of human organs, tissues, and cells should be unpaid and seen either as a moral duty or public welfare service. In certain aspects, this view is in line with the dominant position in contemporary discussions within the Islamic tradition, which prohibited commercializing parts of human body for the sake of organ transplantation. This standpoint rests on a fundamental principle in Islam stating that one does not own his/her hum body because the actual owner is the Creator of the body, namely God. However, would this line of argumentation about essential human body parts like heart and kidney apply in the same way to human biosamples like saliva and other materials usually considered waste like dead skin and poop?

The advocates of the second and opposite view argue for the existence of a property right over one's human bodily material. According to the proponents of this view, denying participants in scientific research property right over their biological material can be a source of unfairness to them. Certain aspects of this view can be accommodated within the Islamic tradition, especially when the focus will be on the biosamples as human body materials which have been separated from the body. Early Muslim jurists had intensive discussions on the possibility of purchasing such parts (e.g. human milk, sweat, tears, mucus, and phlegm) based on three main elements, two of them relate to the material itself (i.e., purity (*tahara*) and possible utility (*manfa'a*) and the third element is whether making such body parts salable would tarnish one's human dignity. Besides these juristic aspects, the advocates of this view also highlighted the relevance of core ethical values like justice and fairness in distributing the financial benefits resulting from the scientific research conducted on the biosamples. How fair it will be, the

advocates of this view wonder, if none of the financial benefits will go to the ones whose biosamples represented the raw material for the researchers' work. Literature sometimes refer to concrete examples like that of Henrietta Lacks, an African American woman whose tumor cells were used in medical research to create profitable 'immortal cell lines'. Some criticized the discrepancies between the large profits made by companies using Lacks' cell lines and Lacks' family and descendants who in many cases could not even afford health insurance. On the other hand, adopting this view will entail adverse consequences as well. It may jeopardize medical research as a common good, giving too much power to donors or individuals. But if this view was adopted, how can the process of benefit sharing be regulated? Who is going to gain what and on what basis? Further, is it not possible to think of other possibilities, beyond the single-owner option, like joint (semi-)ownership among different stakeholders (e.g. research participant, researcher, the biobank housing the research, funders, government, etc.) or considering some stakeholders as custodian or steward (*mu'taman*) and others as semi-owners? Finally, is it possible to differentiate between owning the biosamples on one hand and owning the resulting data on the other hand and state that owning or having authority on the former does not necessarily apply to the latter?

Concluding Remarks

The list of questions mentioned above is by no means exhaustive. There are many further examples that also lend themselves to thought-provoking and critical questions. Thus, submissions on any other related examples, as long as they fall within one of the abovementioned three themes, are welcome. What we do care about is that the submissions will include in-depth and critical analysis of how Islamic ethics can contribute to these discussions.

Those interested in more background information about the intersection of Islamic ethics and genomics can consult the Background Paper of the CILE seminar "Islamic Ethics and the Genome Question", held last year on 3-5 April 2017. Please note that papers submitted for this international conference should focus on the abovementioned three themes only, without repeating the issues discussed in the last year's CILE seminar.

Practical Information

In collaboration with the Research Center for Islamic Legislation and Ethics (CILE), Qatar Genome Programme (QGP) will organize an international conference on the Policies, Regulations, and Bioethics of Genomic Research. This is a two-day conference which will take place in Doha, Qatar on 11-12 April 2018. The second day of the conference will be dedicated to the Islamic bioethical perspectives.

Scholars, academics and researchers are invited to submit their research papers on the three themes which will be addressed during the second day of the conference. Submitted papers will be reviewed and the selected papers will be part of a peer-reviewed publication project.

NOTE: In order to make sure that your submitted paper will fall within the scope of the conference, please read the attached Background Paper carefully before you start working on the paper.

Benefits:

Authors whose papers are accepted for the conference will be offered the following:

- Joining the refereed publication plan of the proceedings of the conference.
- Translating the submitted papers into Arabic or English.
- Covering the travel and accommodation costs during the two days of the conference.

Submission & Deadline

Those who are interested should send

(A) A brief biography (max. 500 words) outlining the applicant's academic background, main research interests and key publications.

(B) Full paper (6000-7500 words), not later than **10 March 2018.** We accept papers written in either Arabic or English. *Please note* that submissions received after this deadline can still be considered for the publication plan, but the authors will not be invited for the conference.

Submissions should be sent to submit@cilecenter.org. For any inquiries about this call-for-papers or about the accompanying Background Paper,

please contact Dr. Mohammed Ghaly (mghaly@hbku.edu.qa) who directs the CILE research unit 'Islam and Biomedical Ethics'.