

CHAPTER FOUR

GENE HUNTING, GENETIC TESTING, AND GENETICALLY TAILOR-MADE DRUGS

1. DIALOGUE IN GENETIC RESEARCH AND APPLICATION

It is a rather uncontroversial view that geneticists should take responsibility for the direct consequences of their research, i.e. those consequences that appear in the research process itself. For instance, they are responsible for the treatment of human subjects participating in the research. More controversial is the view that geneticists should also take responsibility for the indirect consequences of research, i.e. the consequences of publication. I have argued that they should try to affect applications of their findings made by other people.

With regard to genetic research as well as application, dialogue is of key importance. In genetic research, there must be a dialogue between scientists and human subjects on the nature of the research, risks and benefits. In application, there must be a dialogue between scientists and the general public, politicians, and industrialists, on which uses of the results are ethically acceptable and which are not.

I shall now investigate what dialogue and other aspects of moral responsibility could mean more precisely in different kinds of human genetics research and application. This investigation will continue in the next chapter.

'Responding' and 'Owing'

Mapping and sequencing DNA samples from 'immortalized' cell lines that have been completely separated from their human sources and where all identifiers are irretrievably removed do not pose any serious ethical problems with respect to active participation of human subjects. To be sure, when the DNA is first obtained this must be done with the informed consent of the individuals who participate. But the creation of genetic marker maps, physical maps, and determining DNA sequences is pure laboratory work. No human subjects are directly involved. However, the maps and sequences are important tools for further research aiming at the identification of disease genes and function analysis, and in this latter kind of research active participation from human subjects is indispensable.

In all research involving human subjects, certain ethical problems recur. They are related to the two metaphors constituting the concept of responsibility, namely 'responding' and 'owing'. 'Responding' indicates the need for dialogue between geneticists and research subjects. 'Owing' can be interpreted in terms of fair compensation to the subjects for participation in the research. The ethical problems can also be described as related to commonly accepted ethical principles such as respect for autonomy, respect for integrity, and justice. Obtaining informed consent from human subjects is essential, their privacy should be respected, and the medical information should be confidential. Moreover, justice means that human subjects should be treated fairly. However, what does all this mean in human genetics research? Does human genetics research raise any special problems? I shall argue below that there do arise special problems and that the problems get their special character depending on exactly what kind of genetic research is at hand. As examples I choose genetic linkage studies on families and ethnic groups, and research on genetically tailor-made drugs. In relation to each kind of research I shall focus more specifically on problems of dialogue and to some extent fair compensation, and only briefly indicate other problems raised by the research.

Prototypical and Nonprototypical Cases: Autonomy and Informed Consent

Responsible genetics implies dialogue. A key aspect of dialogue in research is obtaining informed consent. Within the scientific community, there is agreement that as a general principle the consent of human subjects must be obtained before doing research. Let us take a look at the concept of informed consent as applied to research on human subjects in general before we turn to genetics research.

The prototypical case of informed consent in research focuses on the individual research subject and includes four main elements, namely disclosure, understanding, voluntariness, and authorization. In addition, there is a precondition, namely capacity.

(1) *Disclosure*. The giving of information is the first important aspect. In general, information should be given to the individual research subject about the aim of the study, methods to be used, anticipated benefits and risks for the subject, the right to withdraw from the study, and criteria for selection of subjects. Perhaps the most important thing for the researcher is to create an atmosphere where the research subject feels at ease to ask further questions. In this way the specific informational needs of each individual can be met.

(2) *Understanding*. This aspect has been stressed increasingly in recent years. It is generally recognized that it is not enough that the researcher thinks that he or she has given correct and sufficient information. The key question is whether the subject has understood. This can to some extent be checked by putting questions to the potential participant.

- (3) *Voluntariness*. There are many different ways to violate this aspect of informed consent, direct coercion being the most flagrant. But there are, of course, more subtle violations such as different kinds and degrees of persuasion and manipulation. A threat to voluntariness that clinical researchers should be particularly aware of is when they recruit patients for research. In such cases the patients might feel obliged to participate due to a sense of dependence on the physician or a sense of debt or gratitude for the care and treatment given. It can be discussed what should count as coercion, i.e. whether persuasion, subtle forms of manipulation, or dependency should be included. From the perspective of cognitive semantics, it is obvious that the concept of coercion has prototype structure and can be extended more or less far.
- (4) *Authorization*. There might be differences in the quality of the authorization depending on the quality of the disclosure, understanding and voluntariness.
- (5) *Precondition: capacity*. A certain minimum ability to understand and decide for oneself is necessary for the principle of informed consent to be applicable. It is a classical issue of controversy in biomedical ethics whether and under what conditions it is justified to involve children and mentally incapacitated persons in research.

The principle of informed consent can be justified in different ways. The two most common justifications are related to the principle of nonmaleficence and the principle of respect for autonomy, respectively. In the early years of research on human subjects informed consent was commonly justified with reference to the former. Consent was seen as a way of minimizing potential harm. In recent years, however, justification with reference to the principle of respect for autonomy has become the dominating one. Autonomy would be without substance if human subjects do not receive information enough to be able to decide for themselves whether to participate.

Recently, however, the individualistic notion of informed consent has been criticized with reference to genetics. This suggests, in terms of imaginative casuistry, that in genetics research we face nonprototypical cases with regard to informed consent. It is possible that the proper unit of consent is the family, not the individual. It is the autonomy of the family that should be respected. This is so because information about one family member's genes implies information about other family members' genes as well. In the first chapter I showed the metaphorical character of the concept of autonomy. The term was originally used about the self-legislative power of the ancient Greek city-states. This political concept has long been used metaphorically about the self-determination of individuals. Now, we see an extension of the metaphor from individuals to families. This is an interesting conceptual development.

Moreover, the metaphor may be extended even further. In the discussion about genetic studies of different ethnic groups around the world, it has been suggested that 'community consent' should be obtained before the research starts. This community consent presupposes that we can talk about a kind of community

autonomy. This means that we come close to the original meaning of the term, namely the autonomy of the ancient city-states.

Furthermore, autonomy has also been extended to future generations by some critics of germline gene therapy. An argument against germline gene therapy is that it is unacceptable because the consent of future people has not been obtained before the modification is carried out. 'Future generation consent' presupposes 'future generation autonomy'.

In some of the sections below, I shall discuss these new suggestions about informed consent and autonomy. The issue of 'future generation consent', however, I shall leave to the next chapter. But I shall also deal with some other ethical problems raised by genetics research involving human subjects.

2. GENE HUNTING IN FAMILIES

Genetic linkage studies raise special ethical problems largely unanticipated in other research involving human subjects. Most of the problems are related to dialogue in the wide sense: recruitment and consent, withdrawal, consent for new studies, disclosure of results, and publication. It is essential that responsible geneticists use their moral imagination in considering these problems, empathizing with the persons involved and envisioning different alternatives of action. For the most part, I shall stay content with presenting the problems, and refrain from giving any suggestions about their handling. The idea of family consent, however, will be discussed rather extensively, because it raises a key problem with regard to dialogue in this kind of research.

In most genetic family studies the research subjects are recruited from clinical practice settings in which family members have been involved in genetic counseling, and where the family pedigree is at least partially established. As the study progresses more members of the extended family are recruited. At a practical level, this means that blood samples for DNA analysis are collected from all these people.¹

Recruitment and Consent

A key problem in gene hunting targeting families concerns obtaining consent from family members. Should the family members be recruited individually or should the family be recruited as a whole leaving the family's internal dynamics intact? The traditional view on recruitment and consent has focused on individual autonomy. But perhaps this model makes us pose the wrong questions?

A closely related problem concerns who should recruit other family members as research subjects. Should it be the researcher or the family member already involved? This is a delicate matter. It is one thing in a purely clinical context to

¹ Many of the problems analyzed below are discussed in Frankel, Teich (eds.), 1993, and Juengst, 1994.

encourage the individual to contact other family members at genetic risk. This is difficult enough. But it is even more difficult to recruit members to a research study that aims at increased knowledge rather than clinical intervention. It is also obvious that the pressure from other family members to participate constitute a threat to voluntariness.

What about the content of the information given to members of the extended family? Is it acceptable to disclose information to recruited members of the extended family about the disease or disorder under study? If the study concerns a socially sensitive disease or disorder, for example, a psychiatric disorder, this might lead to stigmatization of certain members of the family. Moreover, there is the problem concerning whether to disclose psychosocial risks connected with participation in the study. The medical data obtained through the study might be requested, for example, in insurance. This might lead to discrimination and stigmatization of the research subjects. Participants may also have problems with understanding the psychosocial risks.

All this means that in genetic family studies even the element of authorization becomes problematic. Should it be a matter of individual authorization or should the family as a whole give its authorization? Moreover, is it acceptable to involve children and the mentally incapacitated? Can they be involved without consent? Since they do not have capacity for consent, this means that other ethical principles are relevant. Should a kind of vicarious family consent be obtained?

Withdrawal

Other problems are related to withdrawal from research studies. It is a commonly recognized right of the research subjects to be able to withdraw from the study if he or she wants to. Consent does not mean that it is not possible to change your mind. However, does this right to withdraw from the study oblige the scientist to remove information from the pedigree and discard their DNA stored in the freezer? Moreover, this raises the more general question about who owns DNA samples and genetic information.

The traditional view is that DNA samples, like other donated human biological material, is material over which the research subjects no longer hold a claim. An important objection to this view, however, is that unlike most donated tissue DNA samples in a family collection give them scientific value precisely to the extent that they continue to represent their donors. Without identification they are scientifically worthless. One solution for the scientists could be to discard the DNA samples but retain control over the anonymized genetic information. A problem with this view is that even anonymized information can be recognized.

Consent for New Studies Using Stored DNA Samples?

Responsible Genetics

The Moral Responsibility of Geneticists for the
Consequences of Human Genetics Research

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