The Jewish people: their ethnic history, genetic disorders and specific cancer susceptibility

Inbal Kedar-Barnes¹ and Paul Rozen²

¹ Department of Medical Genetics, Rabin Medical Center, Beilinson Campus, Petach Tikva, Israel; ² Department of Gastroenterology, Tel Aviv Medical Center and Tel Aviv University, Israel

Key words: Ashkenazi, cancer susceptibility, ethnic, genetic diseases, Jews, Oriental, Sephardi

Abstract

The Jews are an ancient and unique group of people linked by language, religion and customs in spite of their major geographical shifts, expulsions, forced conversions and massacres throughout their entire history. As a result of these historical events that led to repeated migration, the Jewish people became dispersed into various ethnic sub-groups. Between these ethnic groups exists heterogeneity, as well as some similarities, to the populations amongst whom they lived. Rare genetic diseases have been reported to be prevalent among the different groups of Jews, which for the most part can be explained by random genetic drift together with intra-familial marriages. In this publication, we will briefly discuss the origin of the various ethnic groups and some of the genetic diseases commonly found in them, with emphasis on the Ashkenazim, their prevalent genetic diseases and cancer susceptibility.

Introduction

This text is meant as an overview to the following publications in this journal on malignancies occurring in the Jewish people. Because of their tradition of intra-religion and intra-community marriage, various specific genetic disorders including some common cancers have become prominent in the Jewish ethnic groups. Today, when discussing the Jewish people and their genetic diseases, it is important to precisely define their ethnic group as each ethnic group has its own unique genetic diseases. To classify these ethnic groups geneticists are usually interested in the country of origin or main regions of residence of the person’s ancestors, in order to classify the Jews as, most commonly, Oriental Jews, Sephardim and Ashkenazim.

How these ethnic groups came about will be briefly described [1]. The Hebrew people can be traced back to the Middle East and the Semitic tribes that resided there more than 4000 years ago. From the Bible we learn that Abraham, the founding father, came to the land of Israel from Ur, an ancient city in Mesopotamia (today’s Iraq) [1]. Over the centuries, the Hebrews became dispersed to different countries to form their own communities as described below.

Oriental Jews

Jews originated in the Middle East [1, 2]. The ancient biblical Israel was occupied by a Semitic population, united by their common religion and tribal allegiances, but surrounded by and interspersed with indigenous and invading tribes and nations. Israel, because of its strategic location on the eastern border of the Mediterranean, historically became the crossroads for numerous invading armies: Egypt from the south, Greece and Rome west from the sea and from the north, Babylon and Persia from the east. Following the Babylonian conquest, about 6–700 B.C.E. many of the Hebrews were exiled to the East (dramatically portrayed by Verdi in his opera Nabucco) and founded the Babylonian or Oriental (known today as Iraqi) Jewry. Some of them then followed the developing trade routes from Iraq northwards to Afghanistan, Kurdistan and Buchara (Uzbekistan), eastwards to Iran, and southwards to Yemen and India. Those who remained in Israel, or returned from exile (about 70 years later) with the permission of Cyrus, King of Persia, remained the Israeli (Palestinian) branch. Following decades of Jewish wars against the control of pagan Rome and in order to try and obliterate Hebrew identity after the first century C.E., the Romans renamed their province of Judea (Israel) as Palestine, after the ancient Philistine invaders from the Greek Islands. Large Jewish communities were established in areas of Greek and Roman influence, such as Alexandria in Egypt, Damascus in Syria and in Rome itself. Islamic civilization became dominant in many parts of this world, but even those Jewish communities speaking Arabic, Greek or Latin maintained the Hebrew language and religion.
Sephardic Jews

During the westward expansion of the Greco-Roman Empires, and later the spreading of Islamic civilization towards Spain, the Oriental Jewry voluntarily, or involuntarily, began migrating westward and formed what is known as the Sephardic (meaning Spanish) Jewry. Following the defeat of the Moslems and ascendency of Christianity in that region (Spain and Portugal), the Jewish community was subjected to the choice of accepting religious conversion or expulsion by the inquisition courts from their country of residence, and about 1490 C.E. the latter moved back eastward and to the south. Some established themselves along the coast of North Africa, where together with other communities along the northern and southern shores of the Mediterranean they developed within the Moslem milieu. Some ex-Spanish Jews established flourishing communities in the Balkans, Greece and Turkey, where they spoke, to this day, a form of old Spanish called Ladino, but used the Hebrew alphabet. They also found refuge in Western Europe, notably Holland and even in the “discovered” North and South Americas in order to escape the long arm of the Inquisition.

Ashkenazi Jews

From the sixth to the ninth century, Jews migrated westward from the Palestinian Branch of the Oriental Jewry, establishing themselves especially in Germany along the Rhine (“Ashkenaz”), also in France and even north to England. They developed a dialect called Yiddish, based on a mixture of old German and Hebrew, but written in the Hebrew alphabet. With the ascent of Christian nationalism and the Crusades, they were forced to convert from their religion or leave, or face annihilation. So, in the 13th–14th century some moved into the Ottoman (Turkish) Empire, but mostly to Eastern Europe, especially Poland and also Lithuania, Belarus, the Ukraine and Russia where they became the largest of the Jewish communities [2]. The term “Ashkenazim” is synonymous with Central and Eastern-European Jewry. Since the 12th century, Ashkenazi Jewish communities lived in isolation from the surrounding population. Denigration of the Jewish religion, a social barrier, language barrier and a physical barrier induced this isolation as they lived in ghettos, subsequently having extensive consanguineous marriages. Paralleling a history of persecution, pogroms and lastly, the Nazi Holocaust, many Jews were exposed to the intellectual enlightenment that followed the Middle Ages. The French Revolution, modernity and liberalism allowed the Ashkenazi Jewish people to move from the environment of European suppression and prosecution to find freedom and self-expression in the new worlds of South Africa, Australia, New Zealand, South and Central America, but especially to North America. Some, following religious and national precepts, returned to the remnants of the Palestinian community.

The “Ingathering of the Exiles”

This is a biblical term used to describe the movement back of the Hebrew people from these far-flung countries of exile to Palestine, the land of Israel [1]. In spite of the forced exile by Rome, some Jews always remained in Jerusalem and Palestine, while those in exile prayed daily towards Jerusalem for peace and for their return to Zion. Over a century ago, some came back voluntarily to the desolation of the Ottoman and then the British Mandated Palestine, from Buchara, North Africa, Sudan, Egypt, Yemen, Iraq, Syria, the Balkans, Eastern and Western Europe and the Americas. In 1948, many others came as refugees after their expulsion from the Islamic world. Thus, the ancient Jewish communities of Iraq, Syria, Lebanon, Yemen, Egypt, Morocco, Tunisia, Algeria, Sudan and Iran, and subsequently, the Indian and Ethiopian Jewish communities were effectively brought to an end. This return to Israel marks the end of millennia of Jewish communities in the Moslem world, Africa, Asia, the Balkans, Eastern and most of Western Europe. They form the united Jewish people of what was Palestine and since 1948, is now modern Israel. Ethnic groups contribute their traditions and habits to the totality of Israel, but differences are rapidly disappearing due to the high rate of inter-ethnic marriages ranging from 33.5% in the immigrants, to 60% of the Israel born [3]. Ethnic specific genetic disorders have become less prominent with this genetic remixing.

Genetic markers among Jews

Genetic studies have in the past, and the present, served as a useful tool for reconstructing the history of various populations. The following is a simplification and summary of Jewish genetics. It is not definitive as there are differences of opinions among the researchers and evolving knowledge of the topic. In 1977, Bonné-Tamir et al. [4] presented their data on the genetic markers of Ashkenazi Jews and found this group to be fairly homogeneous with respect to four categories of genetic markers: blood groups (ABO, MNs, Rh, P, Kell, Duffy and Kidd), red cell enzymes, serum proteins and HLA antigens (HLA A and B loci). With regard to these markers, the Ashkenazim are significantly distant from the European population amongst whom they lived. More recent studies, which involved paternally inherited Y-chromosomes, have shown a common haplotype between Ashkenazim, Sephardim and Lebanese Jews as compared to other populations of Eastern Europe [5]. Hammer et al. [6] studied the non-recombining portion of the Y-chromosome in Jewish and non-Jewish populations from the same areas and found closeness between the Jews and non-Jewish Middle-Eastern population (in particular the Syrians and Palestinians), which supports the hypothesis of a
common Middle-Eastern origin. Further studies of Y-chromosome haplotypes revealed that the geographically separate Kurdish and Sephardic Jews were indistinguishable from one another, while both differed slightly from Ashkenazi Jews [7]. The same authors concluded that Jews are genetically closer to Kurds, Armenians and Turks than to the more southern populations [7]. Mitochondrial DNA (mtDNA) studies were done by Thomas et al. [8] on nine geographically different Jewish groups: Ashkenazim, Indian, Ethiopian, Bukharan, Georgian, Iranian, Iraqi, Moroccan and Yemenite Jews; eight non-Jewish surrounding groups and an Israeli Arab group. They revealed reduced diversity within the Jewish groups as compared with the surrounding populations, together with a wide range of different modal haplotypes found in the different communities indicating female-specific founding effects in the Jewish groups, which may be explained by distinct founder women.

As described before, there were always areas of Jewish ethnic interaction, between Sephardim and Ashkenazim in Holland, England and the Americas. Similarly, both Oriental and Ashkenazi Jews followed trade routes to the Americas and to the areas of influence of the British Empire.

### Genetic diseases prevalent among Jews

More than 20 gene loci have been found to be more prevalent among the Ashkenazim [9]. The first group of genetic diseases to be described included some of the lysosomal storage diseases (LSDs) such as Tay–Sachs disease (TSD), which is probably the most studied of the Jewish genetic diseases [10]. TSD is an autosomal recessive, progressive neurodegenerative disorder, which, in the juvenile form is invariably fatal by the age of three years. The disease is caused by hexosaminidase-A deficiency and the accumulation of GM2 ganglioside in the brain. The causative gene is known as HEXA and two mutations in this gene are found among Ashkenazim and one other mutation is prevalent among French Canadians. As reported by Navon et al. [11], another mutation has also been found among Moroccan Jews. The finding of different mutations between the Ashkenazim and the Moroccan Jews and the absence of these mutations in other populations, suggest that the Ashkenazi Jewish mutations in TSD began after the dispersion of Jews from Israel, about the year 70 C.E. and after the establishment of the Ashkenazi community around the year 1000 C.E. [12]. Other Ashkenazi-associated diseases in the LSD group are Gaucher disease and Niemann–Pick disease involving glycolipids, and mucolipidoses type IV, involving mucolipids. Their carrier frequencies and the genes involved are listed in Table 1. In additions to these diseases, other non-lysosomal storage diseases (NLSDs) have also been found prevalent among this ethnic group and are also listed in Table 1.

In an attempt to describe the forces behind the increased frequency of these conditions in the Ashkenazim, Risch et al. [13] analyzed and compared the two groups of diseases: the LDSs and NLSDs with regards to mutation frequencies, mutation ages and their geographic distributions. Risch et al. found no significant differences between the two groups of diseases in all aspects, thus concluding that random genetic drift and founder effects were responsible for the prevalence of these diseases among the Ashkenazim. These conclusions were argued against by Zlotogora and Bach [14] in the same journal and stated that there is a difference between the two groups and the LSDs each have more

### Table 1. Genetic diseases prevalent amongst Ashkenazi Jews, the carrier frequency and genes involved.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Inheritance</th>
<th>Carrier frequency</th>
<th>Chromosome involved</th>
<th>Gene involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lysoosomal storage diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tay–Sachs</td>
<td>AR</td>
<td>1/30</td>
<td>15q23q24</td>
<td>HEXA</td>
</tr>
<tr>
<td>Gaucher Type 1</td>
<td>AR</td>
<td>1/18</td>
<td>1q21</td>
<td>GBA</td>
</tr>
<tr>
<td>Nieman–Pick Type A</td>
<td>AR</td>
<td>1/80</td>
<td>11p15.1q–15.4</td>
<td>SMPD1</td>
</tr>
<tr>
<td>Mucolipidosis Type IV</td>
<td>AR</td>
<td>1/10</td>
<td>19p13.2–13.3</td>
<td>MCOLN1</td>
</tr>
<tr>
<td>Non-lysoosomal storage diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bloom syndrome</td>
<td>AR</td>
<td>1/100</td>
<td>15q26q13</td>
<td>BLM</td>
</tr>
<tr>
<td>Fanconi anemia C</td>
<td>AR</td>
<td>1/90</td>
<td>9q22.3</td>
<td>FACC</td>
</tr>
<tr>
<td>Canavan</td>
<td>AR</td>
<td>1/59</td>
<td>17pter-p13</td>
<td>ASPA</td>
</tr>
<tr>
<td>Familial dysautonomia</td>
<td>AR</td>
<td>1/30</td>
<td>9q31</td>
<td>IKBBAP</td>
</tr>
<tr>
<td>Familial hyperinsulism</td>
<td>AR</td>
<td>1/89</td>
<td>11p14–15</td>
<td>SUR</td>
</tr>
<tr>
<td>Familial hypercholesterolemia</td>
<td>AD</td>
<td>1/56</td>
<td>1p36–35</td>
<td>LDLR</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia</td>
<td>AR</td>
<td>1/10</td>
<td>6p21.3</td>
<td>CYP21A2</td>
</tr>
<tr>
<td>Familial nonsyndromic deafness</td>
<td>AR</td>
<td>1/25</td>
<td>13q11–q12</td>
<td>GJB2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(connexin 26)</td>
<td></td>
</tr>
<tr>
<td>GSD type 1a</td>
<td>AR</td>
<td>Unknown</td>
<td>17q21</td>
<td>G6PC</td>
</tr>
<tr>
<td>Torsion dystonia</td>
<td>AD</td>
<td>1/2000</td>
<td>9q32–34</td>
<td>DYT1</td>
</tr>
<tr>
<td>Factor XI deficiency</td>
<td>AR</td>
<td>1/190</td>
<td>4q35</td>
<td>F11?</td>
</tr>
</tbody>
</table>

AD – autosomal dominant; AR – autosomal recessive; GSD – glycogen storage disease.
than one equally frequent founder mutation and therefore is probably due to a nonrandom selection process.

Table 2 lists some of the genetic diseases occurring among the Oriental Jews and Table 3 lists the genetic diseases commonly found among the Sephardim.

Cancer susceptibility genes

Overall, the risk for cancer differs between the various Jewish ethnic groups. Some of these differences are probably a result of founder mutations within the cancer susceptibility genes and exposure to specific epidemiological risk factors. Founder mutations have been extensively studied in BRCA1 and BRCA2 genes, which confer an increased risk for breast and ovarian cancer, and the APC gene, which confers an increased risk for colorectal cancer. This risk for colorectal cancer, and the differences in its epidemiology amongst the Jewish ethnic groups, will be presented in detail elsewhere in this journal. Table 4 lists some of the common cancer susceptibility genes amongst the Ashkenazim and their carrier frequencies.

Bloom syndrome and Fanconi anemia

Bloom syndrome and Fanconi anemia are rare autosomal recessive disorders marked by chromosome instability. Bloom syndrome and Fanconi anemia complementation group C (FACC) are especially prevalent in the Ashkenazi Jewish community. A single predominant mutation for each of these conditions has been reported in Ashkenazi Jews – BLM\textsuperscript{ASH} in Bloom syndrome and IVS4 in FACC with a carrier frequency for BLM\textsuperscript{ASH} of 1 in 111 [15] and for IVS4 1/92. These mutations can be found in non-Ashkenazi Jewish individuals, but in extremely low frequency and it has been suggested that the mutations date back as far as 70 B.C.E. when the Israelite population was exiled from Palestine by the Roman Empire and settled in Europe [15]. It is well established that both conditions are characterized by genomic instability in the cells resulting in predisposition to malignancies. For Bloom syndrome, multiple types of cancer have been observed including colorectal cancer and premalignant adenomatous polyps [16]. For FACC, there is an increased risk of developing acute myelogenous leukemia in 15% of patients [17] and a cumulative incidence of 29% risk for solid tumors (by the age of 48 years) mostly of head and neck [18].

Among the non-Ashkenazi Jewish Fanconi anemia patients, four ethnic specific mutations have been identified in the Fanconi anemia complementation group A: 2172–2173insG and 4275delT in Moroccan Jews; 890–893del in Tunisian Jews and 2574C>G in Indian Jews. These four mutations account for 88% of the FANCA alleles in the non-Ashkenazi Jewish Fanconi anemia population [19].

Recently it has been reported that biallelic mutations in the BRCA2 breast/ovarian cancer susceptibility gene, have been associated with Fanconi anemia complementation group D1 (FA-D1), mainly in those expressing truncated BRCA2 proteins. [20]. The occurrence of BRCA2 mutations was also studied by Offit et al. [21] in four kindreds with Fanconi anemia and brain tumors. In four of the five cases of Fanconi anemia the existence of one protein truncating BRCA2 allele is sufficient for partial activity of BRCA2 and manifestation of the Fanconi anemia phenotype. Given the potential risk for an Ashkenazi Jewish couple to be carriers of a BRCA2 mutation and a 25% risk of having a child with Fanconi anemia, the authors suggested genetic counseling for these couples.

BRCA1/2 genes

Two mutations are found prevalent in the Ashkenazim in the BRCA1 gene; the most common is known as 185delAG found in 1% of this population and 1 in 5 Jewish women with breast cancer occurring before the age of 40 years [22]. This mutation was also found in 0.47% of Iraqi Jewish women, unselected for personal or family history of cancer. The majority of the carriers of this mutation among the Jews, Ashkenazim and non-Ashkenazim have a similar allelic pattern, so supporting the theory of a founder effect [23]. This indicates that the

Table 2. Genetic diseases commonly found amongst Oriental Jews.

<table>
<thead>
<tr>
<th>Origin</th>
<th>Disease</th>
<th>Inheritance</th>
<th>Carrier frequency</th>
<th>Chromosome involved</th>
<th>Gene involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yemen</td>
<td>PKU</td>
<td>AR</td>
<td>1/35</td>
<td>Xq24.1</td>
<td>PHA</td>
</tr>
<tr>
<td></td>
<td>(\alpha) thalassemia</td>
<td>AR</td>
<td>1/5</td>
<td>16pter-p13.3</td>
<td>HBA</td>
</tr>
<tr>
<td>Iraq</td>
<td>MJF</td>
<td>AR</td>
<td>1/15</td>
<td>16p13</td>
<td>MEFV</td>
</tr>
<tr>
<td></td>
<td>G6PD (X)-linked</td>
<td>¼ males</td>
<td>Xq28</td>
<td>G6PD</td>
<td></td>
</tr>
<tr>
<td>Iran</td>
<td>DJS</td>
<td>AR</td>
<td>1/7 males</td>
<td>10q24</td>
<td>MRP2</td>
</tr>
<tr>
<td></td>
<td>G6PD (X)-linked</td>
<td>1/7 males</td>
<td>Xq28</td>
<td>G6PD</td>
<td></td>
</tr>
<tr>
<td>Kurdistan</td>
<td>Factor VII</td>
<td>AR</td>
<td>1/40</td>
<td>13q34</td>
<td>F7</td>
</tr>
<tr>
<td></td>
<td>G6PD (X)-linked</td>
<td>1/6 males</td>
<td>Xq28</td>
<td>G6PD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(\alpha) thalassemia</td>
<td>AR</td>
<td>1/80 ((\alpha))</td>
<td>16pter-p13.3</td>
<td>HBA</td>
</tr>
<tr>
<td></td>
<td>(\beta) thalassemia</td>
<td>AR</td>
<td>1/160 ((\alpha))</td>
<td>11p15.5</td>
<td>HBB</td>
</tr>
</tbody>
</table>

common ancestor carrying this mutation appeared prior to the separation of the Hebrews to the different Jewish ethnic groups [24]. The second founder mutation known as 5382insC occurs in 0.1% of Ashkenazi women. Another founder mutation, Tyr978X is found in 1 to 2% of Iraqi-Iranian Jews at increased risk for breast and ovarian cancer [25].

In the \textit{BRCA2} gene, a founder mutation known as 6174delT is found in about 1% of the Ashkenazim [26] and in 24% of Ashkenazi Jewish women with early-onset breast cancer [27, 28]. A founder mutation in \textit{BRCA2} was also described among the Yemenite Jews and known as 8765delAG [29]. Approximately 30% of Ashkenazi Jewish women with breast cancer diagnosed under the age of 40 years carry one of these three founder mutations [30].

\textbf{APC gene}

A variant of the adenomatous polyposis coli gene (\textit{APC}) gene known as \textit{I1307K} is found in 6% of Ashkenazim, was initially described in 28% of Ashkenazim with a personal and family history of colorectal cancer, and was associated with an increased risk for colorectal cancer in Ashkenazi Jews [31]. In a larger study, this variant was also detected in 6% of Ashkenazi Jewish individuals unselected for a personal or family history of colorectal cancer, but only in 10.7% of Ashkenazim with a personal and family history of neoplasia [31]. It also was found in 1.6% of Jews of non-Ashkenazi origin and allele analysis confirmed a founder effect that probably occurred before dispersion to Europe and non-European continents [32]. Israeli Arabs have a lower risk for colorectal cancer as compared to the Jewish population; however, in a cohort study of Israeli Arabs with colorectal cancer, 50 individuals aged < 60 year, from 24 unrelated families, were tested for the presence of the \textit{I1307K} variant and 1 in 3 harbored this variant [33]. This may be explained by the hypothesis of a common Middle Eastern origin, or by the tight clustering within the Middle-Eastern populations [6].

\textbf{MSH2 gene}

A single missense mutation in \textit{MSH2} (1906G → C) was the first founder mutation identified in the mismatch repair genes among the Ashkenazim fulfilling the clinical criteria for hereditary non-polyposis colorectal cancer (HNPCC). In a large population-based study by Foulkes et al. [34], 0.44% of Ashkenazi Jewish individuals with colorectal cancer carried this mutation. These authors also conducted a hospital-based study and found that 1.1% of Israeli Ashkenazi Jewish individuals with colorectal cancer carried this mutation. This mutation accounts for 2 to 3% of colorectal cancer diagnosed under the age of 60, 1 in 3 of HNPCC in Ashkenazi Jewish families who fulfill the clinical criteria for this condition and 7% of colorectal cancer occurring in Ashkenazi Jews aged 40 years or younger, irrespective of family history [34, 35].

\textbf{HMPS/CRAC1 locus}

A large Ashkenazi pedigree, originating from Lithuania and dispersed worldwide, has a dominant colon neoplasia syndrome characterized by late onset, multiple colon polyps of mixed histology and, eventually, colorectal cancer. The antecedent polyps include juvenile-like, hyperplastic and mixed polyps, and serrated adenomas [36]. The genetic perturbation has been localized to 15q13–14 [37]. So far, it has also been found in other Jewish families manifesting also non-colonic neoplasia, but has not been evaluated systematically in the Jewish communities and in non-Jews.

\begin{table}[h]
\centering
\caption{Genetic diseases commonly found amongst Sephardi Jews.}
\begin{tabular}{llll}
\hline
Origin & Disease & Inheritance & Carrier frequency & Chromosome & Gene involved \\
\hline
Libya & FMF & AR & 1/5 & 16p13 & MEFV \\
Libya & Cystinuria & AR & 1/25 & 19q13.1 & SLC7A9 \\
Libya & LGMD & AR & 1/10 & 2p13.1-p13.3 & LGMD2B \\
Libya & CJD & AD & 1/50 & 20pter-p12 & PRNP \\
Morocco & AT & AR & 1/40 & 11q22-23 & ATM \\
Morocco & GSD III & AR & 1/35 & 1p21 & AGL \\
Morocco & FMF & AR & 1/7 & 16p13 & MEFV \\
Morocco & Albinism: oculocutaneous & AR & 1/30 & 17q44-42 & TYR \\
Morocco & FMF & AR & 1/7 & 16p13 & MEFV \\
\hline
\end{tabular}
\end{table}

AD – autosomal dominant; AR – autosomal recessive; AT – ataxia telangiectasia; CJD – Creutzfeldt-Jakob disease; FMF – familial mediterranean fever; GSD – glycogen storage disease; LGMD – limb girdle muscular dystrophy.

\begin{table}[h]
\centering
\caption{Cancer susceptibility genes and the carrier frequencies amongst the Ashkenazim.}
\begin{tabular}{llll}
\hline
Gene & Mutation & Cancer syndrome & Carrier frequency \\
\hline
\textit{APC} & I1307K & Colorectal & 6% \\
\textit{BRCA1} & 185delAG & Breast/ovarian & 1% \\
\textit{BRCA1} & 5382insC & Breast/ovarian & 0.1% \\
\textit{BRCA2} & 6174delT & Breast/ovarian & 1% \\
\textit{MSH2} & 1906G>C & HNPCC & 1% \\
\textit{HMPS/CRAC1} & 15q13-14 & Colorectal & Unknown \\
\textit{BLM} & BLM*55 & Bloom syndrome & 1% \\
\textit{FANCC} & IVS4 & Fanconi anemia & 1.25% \\
\hline
\end{tabular}
\end{table}

\textit{a} Autosomal recessive disorder.
Conclusions

Over their history, the Jewish people have both voluntarily and involuntarily maintained their own identity. Because of discrimination, but mainly because of their religious and lifestyle beliefs, they avoided merging with adjacent pagan peoples or voluntarily accepting the predominant non-Hebrew beliefs in the countries of their residence. Proselytes, converts to Judaism, were not actively sought, but accepted if voluntarily requested.

So, the Jewish genetic pools were very much limited to the local community. For this reason, as in other stable communities such as Iceland, Finlad, etc., certain genetic disorders have been found to be ethnic-specific. This is now changing as a result of intermarriage with non-Jews especially in the USA and Eastern Europe, and inter-ethnic marriages within the Israeli population. This healthy expansion of the genetic pool should eventually reduce the ethnic-specific disease burden of the Jewish population.

Acknowledgements

To Drs C. Legum, Tel Aviv, Sharon Plon, Houston, Wendy Rubinstein, Evanston, for their helpful review of this manuscript.

References


