European Journal of Human Genetics (2003) 11, 207–209

www.nature.com/ejhg

LETTER

Finnish and Swedish genotypes and risk of cancer in Sweden

European Journal of Human Genetics (2003) **11,** 207–209. doi:10.1038/sj.ejhg.5200947

The two neighboring populations, Finns and Swedes are thought to have a different population history in which the Baltic Sea has been a geographic genetic barrier.[1] Based on haplotype analysis of Y chromosome and mitochondrial DNA, the settlement of Finns may have taken place in two waves, an early one by Uralic-speaking Asian settlers and the late one by European settlers, with subsequent population bottle necks.[2–4] On the other hand, Swedes are thought to be of Germanic origin and they show extensive haplotype sharing with Germans and other Scandinavians.[1] The allele frequencies of Finns and Swedes differ from each other but even more markedly from the food-gathering population of Saami, a neighbor to Finns and Swedes residing in Lapland.[5] Finns have been genetically isolated, which has contributed to the enrichment of rare, mostly recessive diseases in the population. Over 30 such diseases have been characterized and many have been caused by identified single-gene defects.[4]

All common cancers are complex diseases of environmental and heritable etiology.[6,7] Although the incidence of cancer differs greatly in different populations, migrant studies have shown that the incidence of cancer moves toward the new host population within one generation.[8–11] Migrant studies could answer the questions about population differences in genetic susceptibility to cancer, assuming that the populations differ in the distribution of genotypes.[12,13] However, as such effects, if present, are likely to be small, their demonstration would be particularly demanding. We believe that analysis of cancer incidence in the first- and second-generation Finns in Sweden would be a test of such a principle: population histories are different, the Finnish immigrant community is the largest in Sweden, and the Swedish Cancer Registry has a high quality and coverage.

Incidence data on cancer in Finland and Sweden were obtained for year 1983–1987 from a Nordic publication,[14] and for three sites that were not included in this publication, from annual reports of the Finnish and Swedish Cancer Registries. We used the nation-wide Swedish Family-Cancer Database to analyze cancer risks in Finnish immigrants to Sweden and in their Sweden-born offspring.[10,11] Note that these earlier studies did not include data on cancer rates in compatriot parents or in their children. Immigrants were included only if they had obtained children in Sweden; the median age at immigration was 21 years for men and 20 years for women. The study included 77 750 Finnish men, of whom 62.5% were married to Finnish women, and 105 644 Finnish women, of whom 46.0% were married to Finnish men. They had 194 767, 0- to 66-year-old offspring born in Sweden. We calculated standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for all main cancer sites but show data only for those 17 sites with some significant differences to Swedes (among parents or offspring), who were the reference group. Among parents, a separate analysis was carried out for Finns married to a foreigner or a compatriot. Among offspring, the risks were considered separately whether one or both parents were Finns. The expected numbers were calculated from 5-year-age-, sex-, tumor type-, region- (large cities, south and north), and period- (10-year band) specific standard incidence rates.[10,11]

Previous migrant studies have shown that cancer incidence in the new host country is close to that in the country of origin.[8] We thus tabulated incidence data for cancer in Finland and Sweden (Table 1).[14] We calculated the incidence ratio for various cancers. Even though the overall ratios were not very different, 1.1 for men (Finnish age-adjusted incidence divided by Swedish incidence) and 0.9 for women, there were larger differences at individual sites: male lung cancer 2.4, testicular cancer 0.5 and cervical cancer 0.5. Stomach cancer showed a high ratio in male (1.6) and female (1.7) Finns. In addition to this site, liver and thyroid cancers were in excess in Finns of both genders. By contrast, colon, rectal, and urinary bladder cancers and melanoma showed a decreased ratio in male and female Finns. We show the average male and female incidence ratio from Table 1 in parentheses after 'cancer site' in Table 2.

SIRs for cancer in Finnish immigrants and in their offspring are shown in Table 2, using native Swedes as a reference. Among parents, cancer in Finnish immigrants was decreased at 13 sites; cancer incidence data were available for 12 of these sites and for all but three sites (small intestine, liver, and bone marrow), the incidence was lower in Finland than in Sweden. At most of these sites there was no large difference whether the Finnish immigrant was married to a foreigner or a Finn, suggesting

Table 1 Age-adjusted incidence rates per 100 000 for cancers in Sweden and Finland in 1983–1987

Cancer sites	Men			Women		
	Sweden	Finland	Finland/Sweden	Sweden	Finland	Finland/Sweden
Salivary glands[a]	0.6	0.5	0.8	0.5	0.5	1.0
Stomach	19.9	31.2	1.6	10.1	17.0	1.7
Small intestine[a]	1.2	1.7	1.4	1.1	0.9	0.8
Colon	27.1	20.0	0.7	23.9	17.4	0.7
Rectum	17.6	14.4	0.8	11.5	9.4	0.8
Liver[a]	4.7	5.8	1.2	4.5	5.3	1.2
Lung	39.4	95.9	2.4	14.4	11.2	0.8
Breast				81.3	74.7	0.9
Cervix				10.9	5.6	0.5
Endometrium				18.5	16.8	0.9
Ovary				19.5	13.9	0.7
Prostate	81.6	61.8	0.8			
Testis	4.2	2.2	0.5			
Urinary bladder	25.6	22.1	0.9	6.8	4.2	0.6
Melanoma	12.7	9.6	0.8	12.3	8.1	0.7
Thyroid gland	2.1	2.5	1.2	4.9	7.1	1.4
Leukemia	5.0	4.7	0.9	4.0	4.0	1.0
Any sites	360.7	389.4	1.1	307.4	275.1	0.9

Age-adjusted to the European standard population.
[a]Adjusted to the world standard population and the data were from 1990.

Table 2 SIR for cancer in Finnish immigrants and their offspring in Sweden

Cancer sites	Incidence ratio (Finland/ Sweden)	Parents								Offspring							
		Finn married to foreigner				Compatriots				One parent Finn				Compatriot parents			
		O	SIR	95% CI		O	SIR	95% CI		O	SIR	95% CI		O	SIR	95% CI	
Salivary glands	0.9	21	**0.63**	**0.39**	**0.97**	10	0.65	0.31	1.20	13	1.11	0.59	1.91	5	2.32	0.73	5.46
Stomach	1.6	408	**1.44**	**1.30**	**1.58**	194	**1.50**	**1.30**	**1.73**	20	1.00	0.61	1.54	3	1.16	0.22	3.43
Small intestine	1.1	27	**0.56**	**0.37**	**0.82**	12	**0.53**	**0.27**	**0.94**	8	1.15	0.49	2.27	1	1.00	0.00	5.73
Colorectum	0.8	747	**0.76**	**0.70**	**0.81**	334	**0.76**	**0.68**	**0.85**	100	0.83	0.67	1.00	17	0.87	0.51	1.40
Liver	1.2	228	**0.93**	**0.81**	**1.06**	79	**0.78**	**0.62**	**0.98**	23	1.08	0.68	1.62	4	1.17	0.31	3.03
Lung	1.6	863	**1.31**	**1.22**	**1.40**	511	**1.54**	**1.41**	**1.68**	45	0.93	0.68	1.24	3	0.57	0.11	1.70
Breast	0.9	2029	**0.90**	**0.86**	**0.94**	702	**0.84**	**0.78**	**0.90**	300	0.91	0.81	1.02	35	0.84	0.58	1.17
Cervix	0.5	375	**0.84**	**0.76**	**0.93**	138	**0.81**	**0.68**	**0.96**	114	0.92	0.76	1.11	19	0.86	0.52	1.34
Endometrium	0.9	335	**0.83**	**0.74**	**0.92**	100	**0.72**	**0.59**	**0.88**	22	0.91	0.57	1.38	2	1.20	0.11	4.40
Ovary	0.7	345	**0.80**	**0.72**	**0.89**	113	**0.73**	**0.60**	**0.88**	52	**0.68**	**0.51**	**0.90**	12	0.96	0.49	1.68
Prostate	0.8	433	**0.71**	**0.64**	**0.77**	267	**0.69**	**0.61**	**0.77**	16	0.82	0.47	1.33	0			
Testis	0.5	41	**0.44**	**0.31**	**0.60**	19	**0.36**	**0.22**	**0.57**	132	0.84	0.70	1.00	31	0.89	0.60	1.26
Urinary bladder	0.8	255	**0.70**	**0.62**	**0.79**	123	**0.64**	**0.53**	**0.76**	25	**0.61**	**0.39**	**0.89**	5	0.92	0.29	2.17
Melanoma	0.7	377	**0.66**	**0.59**	**0.73**	160	**0.58**	**0.50**	**0.68**	214	**0.87**	**0.76**	**0.99**	33	**0.69**	**0.47**	**0.97**
Skin (squamous cell)	n.d.	149	**0.70**	**0.59**	**0.82**	63	**0.64**	**0.49**	**0.82**	25	0.83	0.54	1.23	4	0.82	0.21	2.12
Thyroid gland	1.3	197	**1.21**	**1.05**	**1.40**	89	**1.26**	**1.02**	**1.56**	89	1.20	0.96	1.47	18	1.22	0.72	1.93
Leukemia	1.0	241	0.91	0.79	1.03	89	**0.72**	**0.58**	**0.88**	227	0.97	0.85	1.10	53	0.98	0.73	1.28
Any sites	1.0	7071	**0.88**	**0.86**	**0.90**	3003	**0.85**	**0.82**	**0.88**	1425	**0.90**	**0.85**	**0.95**	245	0.89	0.78	1.01

Bold type: 95% CI does not include 1.00.
n.d.=no data.

that the nationality of the spouse played no large role. In the case of endometrial and testicular cancer and melanoma, a compatriot spouse provided a marginally larger protection than an alien spouse, which may be a chance or an environmental effect, reinforced by shared habits. Stomach, lung, and thyroid cancers were more common among Finns than Swedes, and these cancers also showed a higher incidence in Finland than in Sweden. For lung cancer, the difference was highest among compatriots, which conforms to the pattern of smokers marrying smokers, noted as spouse correlation in lung cancer.[15,16] The overall SIR was 0.88 for a single Finnish parent and 0.85 for compatriot parents, based on 7071 and 3003 cancers, respectively.

Among offspring, the total number of cases were 14 250 and 245 for one and two Finnish parents, respectively, and the total SIRs were 0.90 and 0.89. Partially because of statistical power, far fewer significant findings were observed for offspring than for parents, and all of them showed protection: colorectum (SIR 0.79, borderline significance), ovary (0.68) and urinary bladder cancer (0.61), and melanoma (0.87). Melanoma showed a stronger effect (0.69) when both parents were Finnish, which was an exception among the other sites with significant SIRs from a single Finnish parent; for other sites the SIRs moved close to unity. The effect observed for melanoma may have a cultural explanation. Sun exposure early in childhood and adolescence is considered an important risk factor for melanoma.[17] Finnish immigrant families are used to traveling to Finland for their holidays, and maintain the Finnish melanoma incidence, whereas Swedes opt for sunny southern countries. Although these data are not officially recorded, they are based on many years of personal observation and travel between Sweden and Finland.

In summary, within the limits of the statistical power, the present study on Finns, the largest immigrant group in Sweden, showed no evidence on heritable cancer risks that would have distinguished the Finnish genotypes from the Swedish ones. Most incidence rates in first-degree immigrant Finns can be explained by incidence patterns of cancer in Finland.

Acknowledgements

The Family-Cancer Database was created by linking registers maintained at Statistics Sweden and the Swedish Cancer Registry. The study was supported by the Swedish Cancer Society and King Gustaf V's Jubilee Fund.

Kari Hemminki
Department of Biosciences at Novum, Karolinska Institute
141 57 Huddinge, Sweden

Xinjun Li
Division of Molecular Genetic Epidemiology
German Cancer Research Center (DKFZ)
Heidelberg, Germany

Correspondence to: Kari Hemminki, CNT Novum, 141 57, Sweden. Tel: +46 8 6089243; Fax: 46-8-6081501; E-mail: kari.hemminki@cnt.ki.se

References

1 Rosser ZH, Zerjal T, Hurles ME *et al*: Y-chromosomal diversity in Europe is clinal and influenced primarily by geography, rather than by language. *Am J Hum Genet* 2000; **67**: 1526–1543.
2 Sajantila A, Pääbo S: Language replacement in Scandinavia. *Nat Genet* 1995; **11**: 359–360.
3 Kittles RA, Perola M, Peltonen L *et al*: Dual origins of Finns revealed by Y chromosome haplotype variation. *Am J Hum Genet* 1998; **62**: 1171–1179.
4 Peltonen L, Palotie A, Lange K: Use of population isolates for mapping of complex traits. *Nat Rev Genet* 2001; **1**: 182–190.
5 Kaessmann H, Zollner S, Gustafsson AC *et al*: Extensive linkage disequilibrium in small human populations in Eurasia. *Am J Hum Genet* 2002; **70**: 673–685.
6 Lichtenstein P, Holm N, Verkasalo P *et al*: Environmental and heritable factors in the causation of cancer. *N Engl J Med* 2000; **343**: 78–85.
7 Pharoah PD, Antoniou A, Bobrow M, Zimmern RL, Easton DF, Ponder BA: Polygenic susceptibility to breast cancer and implications for prevention. *Nat Genet* 2002; **31**: 33–36.
8 Parkin DM, Khlat M: Studies of cancer in migrants: rationale and methodology. *Eur J Cancer* 1996; **32A**: 761–771.
9 McCredie M: Cancer epidemiology in migrant studies. *Recent Results Cancer Res* 1998; **154**: 298–305.
10 Hemminki K, Li X, Czene K: Cancer risks in first generation immigrants to Sweden. *Int J Cancer* 2002; **99**: 218–218.
11 Hemminki K, Li X: Cancer risks in second-generation immigrants to Sweden. *Int J Cancer* 2002; **99**: 229–237.
12 Cavalli-Sforza L: The DNA revolution in population genetics. *Trends Genet* 1998; **14**: 60–65.
13 IARC. Metabolic polymorphisms and susceptibility to cancer. *IARC Sci Publ* 1999; **148**: 1–510.
14 Engeland A, Haldorsen T, Tretli S *et al*: Prediction of cancer mortality in the Nordic countries up to the year 2000 and 2010 on the basis of relative survival analysis. *APMIS* 1995; **103**(Suppl 49): 1–163.
15 Hemminki K, Dong C, Vaittinen P: Cancer risks to spouses and offspring in the Family-Cancer Database. *Genet Epidemiol* 2001; **20**: 247–257.
16 Hemminki K, Jiang Y: Cancer risks among long-standing spouses. *Br J Cancer* 2002; **86**: 1737–1740.
17 English D, Armstrong B, Kricker A, Fleming C: Sunlight and cancer. *Cancer Causes Control* 1997; **8**: 271–283.