ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Computers in Human Behavior 23 (2007) 2345–2354

Computers in Human Behavior

www.elsevier.com/locate/comphumbeh

Including genotype information in health surveys

P. Cooley [a,*], C. Seifer [a,1], K.H. Taylor [b,2], J.F. Taylor [c,3]

[a] *Research Computing Division, RTI International,[4] P.O. Box 12194, 800 Park Drive, Research Triangle Park, NC 27709, United States*

[b] *University of Missouri, Department of Pathology and Anatomical Sciences, Columbia, MO 65212, United States*

[c] *University of Missouri, Division of Animal Sciences, 920 East Campus Drive, Columbia, MO 65211-5300, United States*

Available online 22 May 2006

Abstract

In a study that examined associations between single nucleotide polymorphism (SNP) loci within the promoter of the *PRTN3* gene and the autoimmune disease Wegener's granulomatosis (WG), we implemented a self-administered pilot survey that captured participants' demographic data, family relationships, incidence of autoimmune disease among family members, and attitudes about DNA collection. We next integrated the survey and genotype data to test associations between genotype and phenotype, to examine demographic characteristics of WG patients and their families, and to examine the robustness of the data collection approach.

The subjects in this study had previously been diagnosed with WG and were recruited through the North Carolina Wegener's Granulomatosis Association. Those who indicated a willingness to participate in the study were asked to provide the names of biological relatives who might also be willing to participate. *PRTN3* genotype information was obtained from DNA samples collected from the 145 study participants using a noninvasive and self-administered buccal-cell harvesting method.

This manuscript describes a pilot study that was performed to collect information from a sample of patients diagnosed with WG and from their parents and siblings who were disease-free. One of its objectives was to identify problems that might be encountered, and possibly prevented, in larger epidemiological studies. Linking epidemiological and genotype data has the potential to yield extended results that cannot be achieved using data from either source alone. We estimate a total

* Corresponding author. Tel.: +1 919 541 6509; fax: +1 919 541 6178.

E-mail addresses: pcc@rti.org (P. Cooley), cls@rti.org (C. Seifer), taylorkh@health.missouri.edu (K.H. Taylor), taylorjerr@missouri.edu (J.F. Taylor).

[1] Tel.: +1 919 541 6478.

[2] Tel.: +1 573 882 6889.

[3] Tel.: +1 573 884 4946.

[4] RTI International is a trade name of Research Triangle Institute.

0747-5632/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.chb.2006.03.011

burden oversampling estimate of 9%: 2.1% to offset the loss of respondents due to including genotype data and 7.0% due to the effects of using a buccal-cell sample to harvest DNA.
© 2006 Elsevier Ltd. All rights reserved.

Keywords: Survey data collection; Genotype data; Buccal-cell; Wegener's granulomatosis

1. Introduction

Wegener's granulomatosis (WG) is characterized by inflammation of blood vessels in the sinuses, lungs, and kidneys. Like other autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis, no molecular biomarkers are known for WG. The disease is rare, affecting 1 in 30,000–50,000 people. Hoffman et al. (1992) estimated that about 500 new cases are diagnosed in the United States each year. WG has been reported in people from 5 to 91 years of age, but the disease is most prevalent in individuals in their forties and fifties. Eighty-five percent of people with the disease are over age 19, and the mean age of those affected is 41 years. WG affects males and females equally. Ninety-seven percent of WG patients are white; only 2% are black, and 1% are of other races (Wegener's Granulomatosis Association, 2004).

The promise of genetic studies to support a variety of health-related lifestyle improvements has been cited by many (Durfy, 2001). The additional costs borne by the addition of biological studies has also been discussed (Finch & Vaupel, 2001). This manuscript describes a pilot study that was performed to collect information from a sample of patients diagnosed with WG and from their parents and siblings who were disease-free. One of the objectives of this pilot study was to identify problems and pitfalls that might be encountered – and possibly prevented – in larger epidemiological studies.

We examined the survey respondents' attitudes about contributing DNA to studies via the use of buccal-cell samples. Our approach combined the administration of a survey instrument simultaneously with the collection of genotype information. Due to the increasing availability of human DNA polymorphisms, usually in the form of single nucleotide polymorphisms (SNPs), studies that integrate DNA and questionnaire data are likely to increase. One goal of this study was to assess the methods necessary to integrate the survey and genotype data and the feasibility of these methods for implementing larger scale studies.

Here we describe our data and DNA collection methods and present our analysis of the attitudinal component of the questionnaire, including attitudes related to the contribution of DNA samples and practical issues that arose during the self-administered collection of questionnaire data and DNA samples.

1.1. Buccal-cell sampling

The traditional method of collecting DNA samples, venipuncture, is expensive and invasive. However, buccal-cell samples are increasingly used as a source of donor DNA to improve participation rates in molecular studies. The buccal-cell collection method was developed by analysts at the National Cancer Institute (Harty et al., 2000). Not only is it less invasive and expensive than venipuncture, but it can also be self-administered

and samples can be sent through the mail, stored at room temperature for up to 7 days, or frozen for future use. Cells are generally collected using tongue depressors, cytobrushes, or mouthwashes, and are then placed into a storage or DNA extraction buffer. Once the DNA has been extracted, it is used primarily for polymerase chain reaction (PCR)-based assays to examine regions of genes that are expected to be polymorphic among the sampled individuals.

The major concern with the buccal-cell method is the amount of genetic material that can be extracted from the sample (Anchordoquy, McGeary, Liu, Krauter, & Smolen, 2003; Vandenbergh, Anthony, & Whitfield, 2003; King et al., 2002; Witso, Stene, Paltiel, Joner, & Ronningen, 2002). King et al. (2002) found that the "swish and spit" method produced an average yield of 15.8 μg of DNA, sufficient for about 300 PCRs and higher than an alternative cytobrush-based buccal-cell harvesting method. Recently, whole genome amplification of DNA obtained from buccal samples has been shown to produce PCR-based genotypes that are indistinguishable between the original and amplified samples (Thompson et al., 2005). Furthermore, whole-genome amplified DNA has now also successfully been used in a hybridization-based assay using microarray technology to simultaneously produce SNP genotypes on a whole genome scale (Gunderson, Steemers, Lee, Mendoza, & Chee, 2005). Collectively, these studies have demonstrated that the amount of DNA harvested by noninvasive self-mediated collection techniques is not an impediment to the nature or extent of genomic analysis to which the samples may be subjected.

2. Methods

The study included a WG patient group and a control group consisting of the patients' parents and/or siblings. Questionnaires and buccal-cell harvest kits were self-administered, and DNA extracted from the cell samples was sequenced for a 655 base-pair (bp) region harboring the promoter and the first exon of the *PRTN3* gene. This region is known to harbor 8 SNP loci.

2.1. Participant selection

Contact information for 302 WG support group participants was obtained from the North Carolina Wegener's Granulomatosis Support Group. Our goal was to recruit 50 WG patients as the disease group and 150 nonaffected parents and/or siblings of the WG patients as the control group. The participants on the support group list included WG patients as well as their relatives, friends, and doctors. The list also contained the names of several persons who were no longer at the address listed on the WG Support Group roster; at least three of these persons were deceased. Table 1 provides a summary of steps undertaken to establish the study participants. All of the participants listed in the WG support group roster were sent a letter that described the study and invited their participation if they were WG patients. On the initial mail-out the participants were also asked to identify biological relatives (parents and siblings only) who they thought would be willing to participate in the study, complete an eligibility screening form, and sign an informed consent agreement. The principal eligibility requirement for a WG patient was a positive antineutrophil cytoplasmic antibody (c-ANCA) result, which provides a definitive diagnosis of WG (Radice & Sinico, 2005). Eligibility also required a signed informed consent agreement, a

Table 1
Identifying study participants

Controls	Ineligibles	Cases	Ineligibles	Status
302				Initial mail-out
191				No response
111				Mail-out request to sign consent form
	17			Mail returned or deceased
	15			No ANCA confirmed
	13			Unwilling to sign consent statement
	10			Otherwise ineligible
55				Exclusions
56				Signed consent forms – participating patients
		126		Number of possible controls – second mail-out
			28	No response
		98		Signed consent form
			1	Dropped out
		97		Participating controls

biological relative willing to participate in the study control group, and willingness to submit a buccal-cell specimen. The parents and siblings of the WG probands defined the potential control group. Individual letters were sent to potential controls, inviting them to participate in the study, complete an eligibility screening form, and sign an informed consent agreement. Eligibility requirements for the control subjects included no history of WG disease, a signed informed consent agreement, and willingness to submit a buccal-cell specimen. Monetary incentives were not used.

2.2. Questionnaire administration

A brief, self-administered questionnaire addressed the sample population's demographic characteristics and the prevalence of other autoimmune diseases in the family. WG patients were asked to identify the severity of the disease and the frequency of the occurrence of flares – a state in which the disease is active and patients are generally on increased medication. The questionnaire also examined the participants' attitudes about providing DNA samples to studies of this type.

2.3. Buccal-cell kit administration

Buccal-cell kits were sent to all study participants. The kits included a letter explaining the study, a paper-and-pencil questionnaire that could be completed in less than 10 min, a small bottle of mouthwash, and a small wide-neck container for collecting buccal-cell samples. The buccal-cell kits were self-administered with instructions that directed participants to collect a sample by rinsing with a small mouthful of the mouthwash and then spitting into the container. Participants were asked to wait at least 1 h after a meal before collecting the sample. The buccal-cell kits were labeled, mailed, and supplied with return envelopes and postage. At appropriate intervals, members of the study sample were contacted and reminded to send their buccal-cell samples to the sequencing contractor, ACTG Inc., and to send their completed questionnaires to RTI, where the data were keyed into an electronic record.

2.4. SNP genotyping

PCR amplification of a 655 bp fragment of the promoter region of *PRTN3* harboring 8 known SNPs was performed on the buccal-cell-derived DNA samples using the primers 34U and 731R described in Gencik, Meller, Borgmann, and Frick (2000). Each PCR product was sequenced in a single direction, and the sequences for all members of a family were simultaneously aligned using AlignX in the Vector NTI suite (Informax). Six variable SNPs within the promoter region of *PRTN3* reported in dbSNP were identified and scored from the sequence. Genotypes for A-564G and 5 other SNP loci in the WG cases and their control family members were merged with the questionnaire results. The questionnaire data were used to stratify the subject sample to identify subsample (i.e., gender) effects.

3. Results

RTI mailed 155 questionnaires and buccal-cell harvesting kits. Of the 155 questionnaires, 145 (48 cases and 97 controls) were returned. Of the 155 buccal-cell kits mailed, 136 were returned to the sequencing contractor with a sample. However, in 9 instances, no DNA could be extracted from the sample. The 9 participants who contributed unusable buccal-cell samples and 1 other nonrespondent were recontacted and asked to submit a second buccal-cell sample. Six of these participants resubmitted samples, and 5 were usable. Thus, a total of 132 buccal-cell DNA samples were successfully genotyped by the sequencing contractor: 43 cases and 89 controls.

Table 2 summarizes the flow of materials in the data collection process. Of the 145 participants who returned questionnaires, 13 (9.0%) failed to generate a genotype, which provides an estimate of the combined follow-up loss due to adding a genotype requirement to the data collection process and using a buccal-cell harvesting method to obtain the genotype information. In addition to the combined lost-to-follow-up burden, Table 2 provides an estimate of the additional lost-to-follow-up burden imposed by buccal-cell self-administered DNA sampling at 7% (10/142), and the lost-to-follow-up burden resulting from individuals unwilling to contribute a sample at 2.1% (3/145). This burden suggests the level of oversampling required to achieve a target study population sample size. However, this figure is sufficiently low that, in most scenarios, obtaining DNA samples using an invasive

Table 2
Flow of materials and loss to follow-up by stage

Stage	Description	Cases	Controls	Total/weighted averages
1	Questionnaires and buccal-cell kits mailed to eligible participants	56	99	155
2	Questionnaires received	48	97	145
3	Samples received for genotyping	47	95	142
4	No DNA extracted from sample	4	6	10
5	Samples analyzed	43	89	132
6	Total lost to follow-up (%)	23.2	10.1	14.8
7	Buccal-cell burden (%)	8.5	6.3	7.0
8	Burden of genotyping (%)	2.1	2.1	2.1
9	Burden of genotyping using the buccal method (%)	10.4	8.2	9.0

Note. In rows 1–5, the last column indicates totals; in rows 6–9, the last column shows the weighted averages of cases and controls (the weights are the sample sizes).

but supervised blood sampling is not warranted. This result suggests that study scenarios favoring self-administrated buccal-cell sampling require surveys with a sufficiently large respondent population to account for follow-up loss.

3.1. Demographic characteristics

Table 3 summarizes the demographic characteristics of the sample. The sample contained slightly more females than males, and this bias remained when the sample was stratified into cases and controls. More than 96% of the sample identified themselves as white, and more than 70% identified themselves as married. The marriage rate appeared to vary by case and control but was not statistically significant ($P > 0.05$). The average age of 56.7 years for cases did not differ from the average age of 57.9 years for controls ($P > 0.65$), which was slightly older than for the national WG population. The results indicate that the sample was demographically similar to the national WG population in terms of gender and race but not age.

3.2. Attitudes about contributing DNA samples

The questionnaire included items to ascertain participants' attitudes about contributing DNA for study purposes. Study subjects were asked to describe their perceptions of the uses that would and could be made of sample DNA by the medical community. A total of 11.3% of the sample members had previously contributed DNA for genetic studies (25% of cases and 4.3% of controls), and only 2.8% of the sample participants held reservations about contributing DNA to genetic studies (2.1% of cases and 3.2% of controls).

Participants were also asked to respond to five statements about the use of DNA in scientific studies by assigning a measure of belief in the accuracy of each statement. Responses conformed to the following 4-point scale: (1) strongly agree, (2) agree, (3) disagree, and (4) strongly disagree. Participants could also indicate that they did not know the answer or did not have an opinion. Table 4 identifies the distributions of the responses to the five attitudinal statements. Table 4 also identifies differences in the distribution of responses for cases versus controls. In all five statements, the distribution of responses between cases and controls was not statistically significant ($P > 0.05$). The exception was the response to statement 5, "Employment agencies or companies that I apply to

Table 3
Demographic characteristics of WG study participants

Description	Total	Cases	Controls	% Cases	% Controls	Pr > Chi
Total	145	48	97	33.1	66.9	NA
Females	77	27	52	34.2	65.8	0.7638
Males	66	21	45	31.8	68.2	0.7638
Married	102	38	64	37.3	62.7	0.1051
Not married	43	10	33	23.3	76.7	0.1051
White	139	46	93	33.1	66.9	0.8340
Non-white	6	2	4	33.3	66.7	0.8340
Average age	57.5	56.7	57.9	NA	NA	0.6542[a]

NA = not applicable.
[a] For average age, $Pr > |t| = 0.6542$.

Table 4
Attitudinal statements about DNA use and study participants' attitudes and perceptions toward DNA sampling

Statement	Group	Strongly agree	Agree	Disagree	Strongly disagree	*N*	Pr > Chi
The use of DNA in diagnosing medical problems will, in the near future, become commonly used by the medical community	Cases	23 (51.11%)	18 (40.00%)	4 (8.89%)	0 (0%)	45	0.9566
	Controls	41 (53.25%)	36 (46.75%)	0 (0%)	0 (0%)	77	
Doctors are able to determine, from my DNA, the appropriate drug they should be treating different diseases with	Cases	8 (19.05%)	20 (47.62%)	13 (30.95%)	1 (2.38%)	42	0.2718
	Controls	10 (13.51%)	50 (67.57%)	14 (18.92%)	0 (0%)	74	
Because DNA reveals so many personal secrets about an individual's medical status, it should be treated with the strictest confidence	Cases	29 (64.44%)	14 (31.11%)	2 (4.44%)	0 (0%)	45	0.3277
	Controls	59 (75.64%)	18 (23.08%)	1 (1.28%)	0 (0%)	78	
Medical insurance companies are likely to use the results of analyzing my DNA to deny medical coverage to me	Cases	8 (17.78%)	21 (46.67%)	13 (28.89%)	3 (6.67%)	45	0.3945
	Controls	17 (22.67%)	30 (40.00%)	27 (36.00%)	1 (1.33%)	75	
Employment agencies or companies that I apply to are likely to use the results of analyzing my DNA to deny me employment opportunities	Cases	5 (11.11%)	14 (31.11%)	18 (40.00%)	8 (17.78%)	45	0.0406
	Controls	3 (4.11%)	25 (34.25%)	42 (57.53%)	3 (4.11%)	73	

are likely to use the results of analyzing my DNA to deny me employment opportunities." The cases tended to report a higher percentage of strongly agree and strongly disagree responses than controls even though their average response was about equal (i.e., both groups tended to disagree with the statement).

4. Discussion

Due to the availability of the human genome sequence and a large number of SNP loci, an increasing number of studies that integrate genomic data with questionnaire data can be anticipated. The technical and computational resources necessary to accomplish the task are readily available. The potential of self-administered DNA collection enhances the feasibility of the process. However, the integration of questionnaire data and DNA collection raises issues associated with collecting genotype data using a buccal-cell harvesting method.

4.1. Costs

Because DNA harvesting is an extra step in the research process, it increases costs. However, the costs associated with a self-administered method based on buccal-cell collection are much lower than for the collection of sera. The self-administered method requires only the cost of the buccal-cell kits, which includes return postage; it was less than $9 per sample in this study. The bulk of the remaining costs included the DNA extraction, PCR amplification of a 655 bp amplicon harboring the *PRTN3* promoter, sequencing of the PCR product, and management of the sequence data. Genotyping or sequencing costs depend on the number of loci and genotyping platform used or the size of the genomic region to be sequenced. In this study, we genotyped 8 SNP loci simultaneously by sequencing a 655 base pair genomic region through subcontract to a commercial company for $50 per sample.

4.2. Sample adequacy

Our study failed to obtain usable DNA in 10 out of 142 extractions (7%). However, 5 successful sequences were generated from resubmitted samples, whereas 2 resubmitted samples yielded no DNA, presumably due to the subjects' continued failure to follow the buccal sample collection directions.

4.3. Other sources of error

During the follow-up of a case that provided inconsistent questionnaire responses, we discovered that the person who had signed the consent form was not the same person who had answered the questionnaire and contributed a DNA sample. The spouse of the person diagnosed with WG had supplied the questionnaire and sample. Although this case was detected and resolved, this instance indicates that such sampling errors can occur in any type of self-administered collection. In our case, we may have detected this occurrence and that of other pedigree inconsistencies had the DNA sample provided a set of SNP genotypes that were inconsistent with the family member's (parents/progeny) genotypes. However, the information content of 8 closely linked loci is not sufficiently powerful to resolve pedigree errors. As the cost of SNP genotyping decreases, and because many loci can now be typed within a single multiplexed reaction, future studies may consider performing pedigree verification testing as a means of data quality control in addition to testing associations between specific mutations and disease phenotypes. We conclude that it is necessary to provide a mechanism that identifies pedigree errors as well as whether the correct subject has provided the requested DNA.

4.4. Biological relationship errors

The estimate of paternity errors in American households is 10% (see Ellman, 2003). A study by the American Association of Blood Banks (2001), for example, discovered that in 28.2% of 280,510 blood tests performed to determine paternity in 1999, the man tested was not the child's biological father. This estimate is biased by sample ascertainment, however, because samples were submitted on cases of suspected mispaternity. In our study, paternity was not specifically tested because it was not covered in our IRB statement. However,

it is very likely that mispaternity will be much lower than the population average in studies involving the voluntary recruitment of subjects. We found one case in which a progeny genotype was inconsistent with the genotype of his putative father at 1 out of the 6 variable SNP loci. This may have been due to mispaternity, sample misidentification, de novo mutation, or to PCR/sequencing artifact. One study participant (a WG case) indicated uncertainty as to whether the sibling controls linked to that case were biological relatives. The case participant requested confirmation of paternity, but this was not provided.

This paper describes the results of the data collection procedures used to integrate survey and genotype data in a study of a biomarker for WG. Linking epidemiological and genotype data has the potential to yield extended results that cannot be achieved using data from either source alone. However, additional costs are associated with collecting genotype information and with harvesting the tissue samples for DNA extraction using buccal techniques. We estimate the oversampling required to offset the loss of respondents due to including genotype data to be 2.1% and the effects of using a buccal-cell sample to collect the DNA to be 7.0%, with a total burden oversampling estimate of 9%.

People willing to provide DNA samples for scientific research may produce a sample that is not representative of the general population, but they may well be representative of the populations in which serious diseases with a genetic basis are segregating. We could not estimate the number of persons unwilling to participate in the study. The initial list of 302 persons obtained from the Wegener's Granulomatosis Support Group list included a number of persons who were ineligible for the study. It also included an unknown number of persons who participated in the study as controls. Consequently, the residual 191 no-response category in Table 1 does not accurately estimate the number of persons unwilling to participate, which is likely to be the same order of magnitude as the response category.

With this caveat, the results of the attitudinal survey suggest that potential subjects are willing to contribute their DNA to support studies of this type as long as appropriate safeguards are available to limit the results of the DNA analysis to the study in question. Sample individuals were well aware of the personalized medicine implications of collecting DNA for diagnosing medical problems and indicated that an individual's genotypic information should be held in the strictest confidence. They believe that medical insurance companies are not to be trusted with their genotype information. Thus, their agreement to participate in this study suggests that they believe that scientific studies of this type maintain acceptable confidentiality practices. Given the selection criteria, it was not surprising to discover that the patients and their relatives who took part in the study hold the views reported. Consenting to provide DNA samples was necessary to take part in the study, so those with strong objections excluded themselves at the outset.

References

American Association of Blood Banks (2001). Annual report summary for 1999. Parentage Testing Standards Program Unit, Bethesda, MD. Retrieved March 10, 2004. Available from: http://www.promega.com/geneticidproc/ussymp11proc/paternity_minisymp/baird.pdf.

Anchordoquy, H. C., McGeary, C., Liu, L., Krauter, K. S., & Smolen, A. (2003). Genotyping of three candidate genes after whole-genome preamplification of DNA collected from buccal cells. *Behavior Genetics, 33*, 73–78.

Durfy, S. (2001). Ethical and social issues in incorporating genetic research into survey studies. In C. E. Finch, J. W. Vaupel, & K. Kinsella (Eds.), *Cells and surveys: Should biological measures be included in social science research? Committee on Population, Commission on Behavioral and Social Sciences and Education, National Research Council* (pp. 303–328). Washington, DC: National Academies Press.

Ellman, I.M. (2003). *Science and legal policy: the case of paternity*. Retrieved September 22, 2005. Available from http://www.law.asu.edu/Files/News/Forum/2003/Jun03/Jun03FORUM.pdf.

Finch, C. E., & Vaupel, J. W. (2001). Collecting biological indicators in household surveys. In C. E. Finch, J. W. Vaupel, & K. Kinsella (Eds.), *Cells and surveys: Should biological measures be included in social science research? Committee on Population, Commission on Behavioral and Social Sciences and Education, National Research Council* (pp. 1–8). Washington, DC: National Academies Press.

Gencik, M., Meller, S., Borgmann, S., & Frick, H. (2000). Proteinase-3 gene polymorphisms and Wegener's granulomatosis. *Kidney International, 58*, 2473.

Gunderson, K. L., Steemers, F. J., Lee, G., Mendoza, L. G., & Chee, M. S. (2005). A genome-wide scalable SNP genotyping assay using microarray technology. *Nature Genetics*, Retrieved April 17, 2005. Available from: http://www.nature.com/ng/journal/v37/n5/abs/ng1547.html.

Harty, L. C., Garcia-Closas, M., Rothman, N., Reid, Y. A., Tucker, M. A., & Hartge, P. (2000). Collection of buccal cell DNA using treated cards. *Cancer Epidemiology, Biomarkers and Prevention, 9*, 501–506.

Hoffman, G. S., Kerr, G. S., Leavitt, R. Y., Hallahan, C. W., Lebovics, R. S., Travis, W. D., et al. (1992). Wegener granulomatosis: an analysis of 158 patients. *Annals of Internal Medicine, 116*, 488–494.

King, I. B., Satia-Abouta, J., Thornquist, M. D., Bigler, J., Patterson, R. E., Kristal, A. R., et al. (2002). Buccal cell DNA yield, quality, and collection costs: comparison of methods for large-scale studies. *Cancer Epidemiology, Biomarkers and Prevention, 11*(11), 1130–1133.

Radice, A., & Sinico, R. A. (2005). Antineutrophil cytoplasmic antibodies (ANCA). *Autoimmunity, 38*, 93–103.

Thompson, M. D., Bowen, R. A., Wong, B. Y., Antal, J., Liu, Z., Yu, H., et al. (2005). Whole genome amplification of buccal cell DNA: genotyping concordance before and after multiple displacement amplification. *Clinical Chemistry and Laboratory Medicine, 43*, 157–162.

Vandenbergh, D. J., Anthony, K., & Whitfield, K. E. (2003). Optimizing DNA yield from buccal swabs in the elderly: attempts to promote cell growth in culture. *American Journal of Human Biology, 15*, 637–642.

Wegener's Granulomatosis Association (2004). The incidence of WG. Retrieved March 10, 2004. Available from http://www.wgassociation.org/aboutwg/statistics.shtml.

Witso, E., Stene, L. C., Paltiel, L., Joner, G., & Ronningen, K. S. (2002). DNA extraction and HLA genotyping using mailed mouth brushes from children. *Pediatric Diabetes, 3*, 89–94.