ego, CA). These were tested on 4 cases involving related living-donor kidney transplants, which we have previously examined for the presence of STR loci (4). For our current analysis, urinary DNA was extracted from 1 mL of recipient urine by commercial column technology (Roche) (9) and eluted in 50 μL of elution buffer, of which 3 μL was used for the subsequent PCR re-

action. This amount corresponds to more than 3000 genome-equivalents of CF-DNA/mL of urine in these samples, which had collected within 24 h of transplantation (2, 4).

SNP loci were analyzed by the MassEXTEND MassARRAY® assay (Sequenom) (6, 7). Genotyping of the donor–recipient pairs, performed on 4 ng of genomic DNA, indicated that in only 16 instances was the donor SNP allele absent from the recipient genome (Table 1). The pertinent donor SNP allele was detected in each of these 16 instances with allelic differences (Table 1). Four representative traces are illustrated in the figure that accompanies the online version of this letter at http://www.clinchem.org/content/vol51/issue9/.

Our data therefore suggest that the analysis of such SNP markers by MS may provide a new alternative for the detection of donor-derived CF-DNA. The accuracy of this approach will, however, have to be examined in a larger scale study and include samples taken at later postoperative stages, when the concentrations of urinary CF-DNA are lower than those examined in this study (2). In addition, it remains to be determined whether this MS approach will permit the reliable quantification of donor SNPs in urinary CF-DNA. As donor-derived CF-DNA has been found in the plasma of other organ transplantation recipients (10), this approach may be useful for the monitoring of transplant rejection in these patients as well.

References


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Performance Characteristics of 6 Third-Generation Assays for Thyroid-Stimulating Hormone

To the Editor:

A recent report in this journal by Rawlins and Roberts (1) compared 6 commercial third-generation assays for thyroid-stimulating hormone (TSH). The authors reported a functional sensitivity of 0.039 mIU/L for the ADVIA Centaur® TSH-3, in contrast to the manufacturer’s claim of 0.019 mIU/L (2). Rawlins and Roberts (1) cited a single earlier ADVIA Centaur study (3), which they claim agrees with their results; however, the cited study actually evaluated the ADVIA Centaur TSH, a second-generation TSH assay that is different from the TSH-3. Previous publications on the ADVIA Centaur TSH-3 reported functional sensitivities in the range of 0.018–0.025 mIU/L (4–6) and are in general agreement with the manufacturer’s claim. We investigated further to resolve the apparent inconsistencies raised by Rawlins and Roberts (1).

We conducted a new evaluation of the functional sensitivity of the ADVIA Centaur TSH-3. Included were the same two lots used by Rawlins and Roberts (lots 26 and 29), which now had been expired for 8–9 months, as well as two in-date lots (lots 38 and 41). The method closely followed that of Rawlins and Roberts (1). Serum samples were used to prepare 8 patient pools distributed within the TSH-3 dose range of ~0.01–0.15 mIU/L.

Pools were tested on one ADVIA Centaur with each TSH-3 lot in duplicate, twice per week, for 3 weeks, for a total of 12 replicates. Each pool was tested with all TSH-3 reagent lots in one run to allow all results to be generated within several minutes. The Centaur was a routine production system used for various assay and patient sample evaluations in support of Centaur customers. Functional sensitivity was determined by plotting the total CV for each of the 8 pools as a function of TSH dose. The data were fit with a power equation of the form Total CV = a(TSH dose)b,

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and functional sensitivity was calculated to be the dose in the equation with a total CV of 20%. We found the functional sensitivity, using reagent lots 26 and 29, to be 0.012 mIU/L. This value is considerably lower than that of Rawlins and Roberts (1), although the same reagent lots were used. For the two newer in-date lots, functional sensitivity was calculated to be 0.022 mIU/L. Both determinations are consistent with the manufacturer’s claim of 0.019 mIU/L for the ADVIA Centaur TSH-3.

In summary, we believe that the data support our functional sensitivity claim for the third-generation ADVIA Centaur TSH-3 method and that this claim has been demonstrated in other studies (4–6).

References

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Dr. Roberts responds:

To the Editor:

We appreciate the information provided by Waskiewicz et al. in their letter. They are correct that the study by Ognibene et al. (1) refers to a second-generation thyrotropin (TSH) assay on the ADVIA Centaur and not to a third-generation TSH assay. We regret this error. The study by Vogeser et al., cited as Ref. 4 by Waskiewicz et al., did not actually include an estimate of the functional sensitivity, but rather imprecision was 22.3% at a TSH concentration of 0.014 mIU/L and 3.9% at 0.26 mIU/L (2). These are not sufficient data to estimate functional sensitivity.

The major issue is why our study yielded a higher functional sensitivity than theirs did. They indicate that each pool was tested with all reagent lots in one run. Our study used each of two reagent lots sequentially, which might in part account for the higher imprecision (3). The instrument in their study was used for various patient sample evaluations in support of Centaur customers. The instrument in our study was used for routine testing of patient samples in a reference laboratory setting with ~10 000 patient results reported monthly, and TSH-3 was one of the analytes being routinely reported. The differing environments and use of the ADVIA Centaur analyzers in these 2 studies may have contributed to differences in imprecision. We maintain that our experimental conditions are more representative of what will be encountered in routine clinical testing.

It is unclear whether authors of previous studies have performed imprecision studies in a research setting or in a clinical testing environment. To our knowledge, no one has reported on the effects of increasing workload on assay imprecision, but this may be a factor affecting the precision of some analyzers. A better understanding of which variables are most important and how they affect assay imprecision could lead to better assay performance during routine clinical use. In the study by Waskiewicz et al., the functional sensitivity of lots 38 and 41 of TSH-3 reagent was 0.022 mIU/L, whereas that of lots 26 and 29 (the ones used in our study) was 0.012 mIU/L. It would be interesting to field-test lots 38 and 41 to see whether the increased functional sensitivity exhibited by these two lots in a controlled setting would also be evident in routine clinical testing.

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The Biological Variation of C-Reactive Protein in Polycystic Ovarian Syndrome

To the Editor:

An inverse relationship between increased C-reactive protein (CRP) concentrations and insulin sensitivity has occurred in individuals with polycystic ovarian syndrome (PCOS) (1) and is thought to contribute to an