Physical location and linked genes of common forensic STR markers

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Abstract. There is increasing evidence for a phenotypic role of junk DNA such as STRs. As phenotypic effects of forensic DNA markers are highly undesired, it seems to be worthwhile having a detailed view of the physical location and linkage to genes or diseases for all STR markers used in forensics. Herein the results of a search in genetic databases for 13 loci for which such details are not given in the literature are presented. © 2002 Published by Elsevier B.V.

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1. Introduction

It is good forensic laboratory praxis (and in Germany even required by law) to use DNA polymorphisms without association to a disease or other phenotypic effects. Therefore, noncoding STRs, which, like other “junk DNA” structures, were always regarded as neutral genomic elements, were selected for forensic purposes. However, in the last years the role of “junk DNA” has seen a dramatic change: at present, there is gathering evidence for an active role of STRs in gene regulation via interaction with transcription factors [1,2]. Even the assumption that variable tetrameric repeat systems are always noncoding polymorphisms is questioned: Wren et al. [3] showed that about 8% of tandem repeats are located in the coding regions and thus can potentially lead to frame shifts causing diseases.

These results have prompted the editors of Science Magazine to rank the discovery of the relevance of “junk DNA” as number 5 “Breakthrough of the year 2004” in scientific
research—the second highly ranked life science topic, beaten only by cloning of primates [4].

For many STRs of forensic relevance exact physical localization and potential gene and disease linkage are unknown to forensic scientists. Nevertheless, this information would be valuable to assess the risk of potential phenotypic effects. This reasoning has already been undertaken for some loci: For TH01, e.g., it is known that it is located in intron 1 of the tyrosine hydroxylase gene on the short arm of chromosome 11 (11p15.5), and closely linked to the insulin gene and the Harvey ras 1 oncogene. These facts have elicited further genetic studies which found that either by linkage to one of these genes or by direct influence on the gene regulation that the allele 9.3 seems to be associated to diseases such as hypertension and psychosis [1]. As such phenotypic effects of STRs are highly undesirable in forensic sciences; it appears to be worthwhile to investigate the current extent of information about forensic STR loci in common genetic databases.

2. Materials and methods

For 13 loci (Fig. 1) without detailed information in the forensic literature, an in silico search in the UniSTS database for the exact physical location was performed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=unists). Moreover, the Ensembl database was searched to verify that the STRs are noncoding polymorphisms (http://www.ensembl.org/Homo_sapiens/index.html). Finally the OMIM database was searched for linkage between markers and inherited diseases (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=omim).

Fig. 1. Exact physical location of 13 STR markers: D2S1338 (q35), D3S1358 (3p21.31), D5S818 (5q23.2), D7S820 (7q21.11), D7S1517 (7q31.33), D8S1179 (8q24.13), D8S1132 (8q23.1), D12S391 (12p13.2), D13S317 (13q31.1), D16S539 (16q24.1), D18S51 (18q21.33), D19S433 (19q12), D21S11 (21q21.1).
3. Results and discussion

For all markers the exact physical location was found (Fig 1).

Moreover, whereas no marker was localized in a coding region, 4 markers were located in introns: D3S1358 in intron 20 of the leucyl-tRNA synthetase 2 gene, D7S820 in intron 15 of the semaphorine 3A gene, D18S51 in the B cell lymphoma 2 (Bcl-2) gene and D7S1517 in the hyaluronoglucosaminidase 4 gene.

As an example, the region surrounding D3S1358 is given in Fig. 2. Details for the other loci can be requested from the authors.

A search in the OMIM database for known linkage between diseases and markers revealed that D8S1179 was linked to Meckel syndrome (type 3) in an Indian family. D18S51 is linked to polyostotic osteolytic dysplasia (McCabe disease). D2S1338 is linked to familial pseudohyperkaliemia 2. All these diseases are extremely rare inherited disorders, and linkage does not necessarily allow the conclusion that typing these markers would infer the undesirable diagnosis of an inherited disorder.

Our results allow the reassuring conclusion that all markers are noncoding markers and that, up to now, for none of these 13 markers, significant influences on the phenotype are known.

References