and the filament formation of purified recombinant mutant desmin was analysed *in vitro* by atomic force microscopy (AFM), as previously described.[4]

To our surprise, the expression of desmin-p.P419S does not induce an aggregation in either cell line as recently described for other ARVC-related desmin mutants[4–6] (Figure 1). The cell culture data were also supported by the AFM analysis virtually yielding undistinguishable desmin filaments between wild-type and desmin-p.P419S *in vitro* (Figure 2). Thus, our data reveal that the desmin mutant p.P419S published by Hedberg *et al*[1] forms filaments *in vitro* and in transfected cells. Consequently, it might be important to look for further molecular triggers, which induce or influence the protein aggregation in the Swedish patients suffering from MFM/ARVC. From our point of view, the next-generation sequencing data of Hedberg *et al*[1] might provide an important basis for further studies, identifying modifier genes or other molecular abnormalities responsible for desmin aggregate formation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Reply to Brodehl *et al*

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We appreciate the comments by Brodehl *et al*[1] on our recent article describing a *DES* mutation in a family with myofibrillar myopathy and arrhythmogenic right ventricular cardiomyopathy.[2] We would like to clarify that the mutation, p.P419S in the desmin gene (*DES*), indeed co-segregates with the disease. When we compared the muscle biopsy findings with the presence of the p.P419S *DES* mutation, desmin storage was found in all investigated family members with the *DES* mutation but not in those without the mutation. The clinical expression of the disease was highly variable within the family. The original linkage study on this family was based on combined findings from clinical examination, electromyography and muscle biopsy.[3] Three of five asymptomatic individuals were incorrectly considered affected by the myopathy based on these investigations. These three individuals showed only mild and unspecific myopathic changes and no desmin storage. Whether these individuals were affected by another mild myopathy remains to be clarified. These results demonstrate diagnostic difficulties with some forms of dominantly inherited muscle diseases, as they can display a wide clinical and morphological variability even within a given family.

In conclusion, despite the report by Brodehl *et al*[1], we believe that the identified desmin mutation is causative for the diseases in our family, as it segregates perfectly with desmin storage in muscle. Further support for this conclusion is the finding of the same mutation segregating with desminopathy in a Spanish family.[4]

CONFLICT OF INTEREST

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