# MRC Holland Support



# Do mismatches between probes and their target sequences influence MLPA and digitalMLPA results?



Probes can be affected by mismatches between the probe sequence and the sample DNA. The presence of one or more mismatches can lead to a reduced probe signal, which can mimic a deletion. As this is also the case for non-pathogenic variants, such as SNVs, it is very important to confirm single-probe deletions. Read more about confirming results in this article.

# Background

Mismatches can have different effects depending on their position in the probe's target site.

- Mismatches at the ligation site always disrupt the ligation of the two probe oligonucleotides to some extent, depending on the type of mismatch. This is what enables the detection of known SNVs with MLPA and digitalMLPA. See this article for more information.
- Mismatches near the ligation site (within ~5 nt) may also decrease the ligation efficiency, which can result in a decreased signal.
- Mismatches further from the ligation site may sometimes have an effect if they destabilize the probe's hybridisation to the sample DNA. This is less likely to be an issue for digitalMLPA probes, as these probes tend to have longer hybridisation sequences than MLPA probes.

When we design probes, we try to avoid frequently occurring variants retrieved from public databases and customer feedback. However, new variants are continuously being discovered, and it is often not possible to avoid all known (rare) variants. For this reason, the possibility of a mismatch should always be considered for a single-probe deletion.

Note
Customer feedback is a very important source of information about the performance of our products in practice. If you find a variant with an effect on one of our probes, please contact us – especially if the variant occurs frequently. We may be able to use this information to improve the probe.

- Tags
- digitalMLPA
- MLPA

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