be developed to obtain resistance against these economically important groups of plant viruses.

In conclusion, accumulating evidence is available that RMR can be obtained to the vast majority of plant viruses, including the (+)- and (–)-stranded viruses, and possibly even DNA viruses.

5. Working Mechanisms of RNA-Mediated Virus Resistance

Despite intensive research, our knowledge on the exact molecular mechanisms by which RMR works is still fragmented. This information is essential in order to predict the long-term stability of such engineered sources of resistance and to further improve this relatively novel technology.

One remarkable property of RMR is that it is only active against homologous viruses. The resistance is overcome by more distantly related viruses. A general rule of thumb is that at least 90% nucleotide sequence homology between transgene and corresponding viral gene is required to obtain resistance ***(13,26,28)***. For this reason, it can be assumed that engineered virus resistance cannot simply be overcome by pathotypes with single or few point mutations in their genome. Assuming that the transgenes behave stably over generations, it can be anticipated that RMR will confer durable virus resistance to crops.

Experiments performed by Lindbo and Dougherty ***(24)*** and Lindbo et al. ***(37)***, using transgenic tobacco plants resistant to tobacco etch or potato Y potyvirus, provided the first hints that RMR is conferred by sequence-specific RNA degradation in the cytoplasm. In vitro run-on labeling experiments using potyvirus-resistant tobacco plants demonstrated that the rate of transcription in the nuclei of resistant plant cells is high, compared with that in nuclei of susceptible transgenic plant cells. In contrast, in the resistant plant cells the steady-state levels of transgenic mRNA are low, sometimes even lower than those in susceptible transgenic plants. This suggests that the transgenic mRNAs (and most likely, also, the homologous RNAs of invading viruses) are selectively and rapidly degraded in the cytoplasm of resistant plant cells. These findings have recently been confirmed for several other plant–virus combinations ***(20,36)***.

As mentioned in the previous subheading, resistance can be obtained by expression of RdRp, MP (or other viral sequences, in case of potyviruses) in plants. However, so far, it has remained unknown which parts of the genes are capable of conferring resistance. Although speculative, it appears that the 5' leader and 3' trailer sequences, and the length of the transgenically produced mRNAs, play important roles.

For most viruses, antisense RNAs are also capable of conferring virus resistance, but this does not seem to hold for all plant viruses. Possibly, the