Supplemental Figure 1. Representative image of the in-gel hybridizations used for G-strand-overhang analysis. (A-B) Representative photographs of in-gel hybridizations: 5µg of liver DNA of non-infected mouse liver (lane 1), Ad TRF2ΔBΔM-infected mouse liver (1x10¹⁰ PFU/ml, lane 2), and Ad GFP-infected mouse liver (1x10¹⁰ PFU/ml, lane 3) was digested over night with *Hinf*1 and size-fractioned by pulse-field electrophoresis in 1% agarose gel. (A) Labeling of the non-denatured gel with [³²P-(CCCTAA)]₃ probe. (B) Re-labeling of the same gel after stripping and denaturisation with [³²P-(CCCTAA)]₃ probe. (C) Ratio of signal intensity of the telomeric smear in the non-denatured gel compared to the denatured gel. Experiments were done in triplicates and the mean value was calculated from the ratio of each experiment.

Supplemental Figure 2. Diagram on the percentage of TRF2ΔBΔM-expressing liver cells in response to the indicated viral titres at day 2 and 7 after virus infection. Note the positive correlation between the percentage of TRF2ΔBΔM-expressing liver cells and the titre of Ad TRF2ΔBΔM used for viral infection.
**Supplemental Figure 3.** Diagrams of the DNA content of liver cells 10 days after Ad GFP (left diagram) or TRF2\(^{ΔBΔM}\)-infection (right diagram). In Ad GFP-infected mice most cells had a DNA content of 2n and a subpopulation of liver cells showed a 4n DNA content. In Ad TRF2\(^{ΔBΔM}\)-infected mice a high rate of liver cells had a DNA content higher than 4n (right side of the red dotted line).

**Supplemental Figure 4.** (A) Representative photographs after Co-staining of TRF2\(^{ΔBΔM}\) expression (top) and TUNEL (bottom) on liver sections 48h after Ad TRF2\(^{ΔBΔM}\) infection. Note the co-localization of TUNEL-positive cells with cells showing high expression of TRF2\(^{ΔBΔM}\). White arrows mark cells with a low TRF2\(^{ΔBΔM}\) expression, which are TUNEL-negative. Orange arrows mark cells with high TRF2\(^{ΔBΔM}\) expression, which are TUNEL-positive (magnification 1000x). (B) Representative photographs after co-staining of TRF2\(^{ΔBΔM}\) expression (top) and SA-β-gal activity in liver sections 48h after Ad TRF2\(^{ΔBΔM}\) infection. Counterstaining was done with DAPI (bottom). The white arrow marks a cell with a low expression level of TRF2\(^{ΔBΔM}\), which shows SA-β-Gal activity. Orange arrows mark cells with high TRF2\(^{ΔBΔM}\) expression, which are SA-β-Gal-negative (magnification 1000x). (F) Histogram showing the distribution of the cellular expression level of TRF2\(^{ΔBΔM}\) among SA-β-gal positive liver cells (left bar column) and among TUNEL-positive liver cells (right bar column) 48h after Ad TRF2\(^{ΔBΔM}\) infection. Liver sections of 5 mice infected with Ad TRF2\(^{ΔBΔM}\) (2x10\(^{10}\) PFU/ml) were evaluated by 2 independent investigators.
**Supplemental Figure 5.** Ad GFP ($1 \times 10^{10}$ PFU) infected mouse liver, 48h after virus infection (left side: GFP; right side DAPI). (A) Negative-control of uninfected mouse liver. (B) Right lateral liver. (C) Right median liver lobe. (D) Caudal liver. (E) Left lateral liver lobe. (F) Left median liver lobe. (Magnification 100x). Note that all liver lobes show a similar rate of infection.
Supplemental Figure 1:

A

Native gel

B

Denatured gel

C

<table>
<thead>
<tr>
<th>Relative G-Strand Overhang Signal</th>
<th>Average ± SD</th>
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<tbody>
<tr>
<td>Control</td>
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</tr>
<tr>
<td>Ad TRF2 (\Delta)M</td>
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</tr>
<tr>
<td>Ad GFP</td>
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Supplemental Figure 3
Supplemental Figure 4