Statistical Analysis

The total number of stem cell divisions in the lifetime of a tissue was calculated as follows. Let s be the total number of stem cells found in a fully developed tissue, with s a power of 2, for simplicity, and no cell death. Starting from the first precursor cell of that tissue, it takes x generations during development to generate all of these cells, where $2^x = s$. Once the tissue has been fully developed, each of these s cells undergoes a total of d further divisions, due to normal tissue turnover, in the lifetime of that tissue. These turnover divisions are assumed to be asymmetric, but note that a balance between apoptosis and symmetric self-renewal would yield the same average number of cell divisions for a tissue in homeostasis. Thus, the cumulative number of division events, each yielding a new stem cell, among all stem cells in a lifetime (*lscd*, for lifetime stem cells divisions), is

$$lscd = \sum_{n=1}^{log_2 s} 2^n \; + s \cdot d.$$

In general, s is not a power of 2, and the use of the floor function to approximate $log_2 s$ may not be appropriate. Noting that the partial sum of the geometric series is equal to $2s$-2, we obtain our formula for *lscd* for a general s:

$$lscd = s\,(2 + d) - 2.$$

The estimates for s and d are provided in Table 1. For each cancer type, $lscd = s\,(2 + d) - 2$ was plotted against the lifetime incidence of that specific cancer type in Fig. 1 of the main text.