6. Mistargeting of AID contributes to B-cell malignancy.

- Burkitt's Lymphoma:
  1. This cancer affects the mature B cells and is predominantly seen in children. It causes a **massive lymphadenoopathy** (swollen lymph nodes), often seen in the jaw due to an accumulation of unproliferated B cells, and is treated by chemotherapy.
  2. It is endemic in Africa, where there are prevalent areas with **chronic malaria exposure** and **Epstein-Barr virus (EBV)** infection.
  3. It is also increased with incidence of HIV infection.
  4. Almost all cases of Burkitt's lymphoma involve over-expression of MYC and is caused by a reciprocal translocation in the **MYC gene on the long arm (q) on chromosome 8.**
  5. Translocation can involve one of three Ig genes, with the most frequent translocation being t(8;14) of the Ig heavy chain gene on chromosome 14, which moves the MYC gene to chromosome 14.
  6. Other translocation variants: t(8;2) and t(8;22) leave MYC on chromosome 8 but place parts of the kappa or lambda Ig **light chains** next to the 3' end of the gene.
  7. The consequence of the typical translocation is that the myc protein is expressed in parts of the cell cycle when it should be switched off.
  8. The translocation event separates MYC from its normal transcriptional promoter and places it under the control of a **highly active transcriptional regulators of an Ig gene.**
  9. This leads to the loss of the normal modulation of MYC expression by physiological signals. Thus, it is **constitutively expressed at high levels** as opposed to the tight control.
  10. Initially, following translocation, MYC is structurally normal but subsequently acquires point mutations.