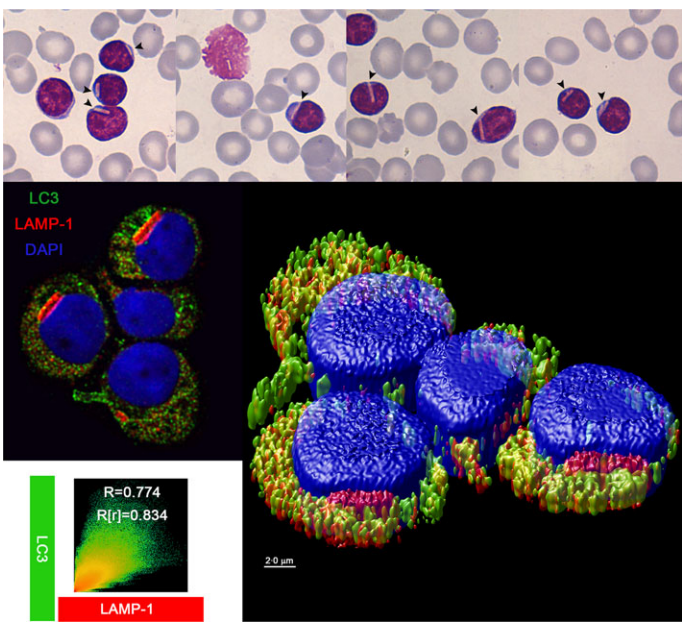
Microtubule-associated protein 1A/1B-light chain 3 (LC3) 'decorates' intracytoplasmic inclusions in a patient with chronic lymphocytic leukaemia



A 77-year-old woman, diagnosed nine years previously with chronic lymphocytic leukaemia (CLL) Rai stage I, was referred to our hospital with disease progression (night sweats, weight loss and organomegaly). Her peripheral blood count showed leucocytosis (WBC 104·9 × 10^9/l; 94% lymphocytes), anaemia (haemoglobin concentration 105 g/l) and a normal platelet count (146 × 10^9/l). The monoclonal B-cell immunophenotype had been determined previously as lambda light chain-restricted, $CD19^+$, $CD20^{dim}$, $CD5^+$, $CD200^+$, $CD22^{dim}$, $CD79b^{dim}$, surface membrane immunoglobulin (sIg)M^{dim}, $CD23^-$, $CD10^-$ and $FMC7^-$. A May-Grünwald-Giemsa-stained blood film showed mature lymphocytes with around 50% of the total lymphocytes containing intracytoplasmic inclusions, seen as rectangular crystalline structures (top). The patient was treated with chlorambucil (unfit patient), several times, obtaining partial remission.

Although inclusions in lymphoproliferative and plasmacytic disorders are not common, many different types have been described (Appendix S1). In CLL they can be present as vacuoles or crystalline, filamentous or Auer-rod-like structures. These aggregates have been shown to contain immunoglobulin, mainly associated with the rough endoplasmic reticulum and, to a lesser extent, lysosomes.

As the autophagy pathway is primarily responsible for the degradation of long-lived or aggregated proteins, we evaluated the presence of the autophagic marker LC3 (which labels autophagosomes) by confocal analysis of cytospin slides from this patient. Interestingly, we observed LC3 puncta 'decorating' the intracytoplasmic inclusions, which colocalized with the lysosomal-associated membrane protein 1 (LAMP-1), suggesting activation of autophagic flux (bottom).

Abnormal autophagic protein degradation has been associated with many human diseases, including cancer. However, whether autophagy dysfunction contributes to the formation of these protein aggregates in CLL cells remains unknown.

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