# TTF-1 expression in diffuse large B-cell lymphoma: a confusing game of clones.

**Ann-Sophie Candaele[1], Mieke Van Bockstal[1,2], Alessandra Camboni[3], Sofie Geenen[1], Lies Vandemaele[1], Frédéric De Ryck[4], Louis Libbrecht[3], Sofie Verbeke[1,2], Jo Van Dorpe[1,2]**

[1] Department of pathology, Ghent University Hospital (Ghent, Belgium), [2] Cancer Research Institute Ghent (CRIG, Ghent, Belgium), [3] Department of pathology, Saint-Luc Hospital (Brussels, Belgium), [4] Department of thoracic and vascular surgery, Ghent University Hospital (Ghent, Belgium).

## Background

Thyroid-specific transcription factor 1 (TTF-1) is a transcription factor encoded by the *NKX2-1* gene. TTF-1 expression is assumed to be restricted to pulmonary and thyroid epithelium.

However, nuclear staining has been described in colorectal cancer, breast cancer, cholangiocarcinoma and adenocarcinoma of the cervix and endometrium, amongst others. This aspecific immunohistochemical staining occurred in both primary tumours and metastases.

Two commercially available monoclonal anti-TTF-1 antibodies are commonly used: SPT24 and 8G7G3/1. The SPT24 clone is suspected to be more sensitive but less specific than the 8G7G3/1 clone.

## Aim of this study

To our knowledge, TTF-1 expression has not yet been described in diffuse large B-cell lymphoma (DLBCL). We encountered an index case of DLBCL expressing TTF-1, which prompted us to investigate TTF-1 expression in a series of DLBCL.

## Materials & methods

Archived paraffin-embedded tissue blocks were retrieved from 106 DLBCL cases, of which 32 were diagnosed at the St Luc Hospital (Brussels, Belgium) and 74 were diagnosed at Ghent University Hospital (Ghent, Belgium).

Immunohistochemistry for TTF-1 was performed on 3,5 µm tissue sections using an automated immunostainer (Benchmark XT, Ventana Medical Systems, Oro Valley, AZ, USA). Two anti-TTF-1 clones were used: the SPT24 clone (dilution 1/20, Novocastra™ liquid mouse monoclonal antibody, Leica Biosystems Newcastle Ltd, UK) and the 8G7G3/1-clone (dilution 1/50, mouse monoclonal, Dako Cytomation, Glostrup, Denmark).

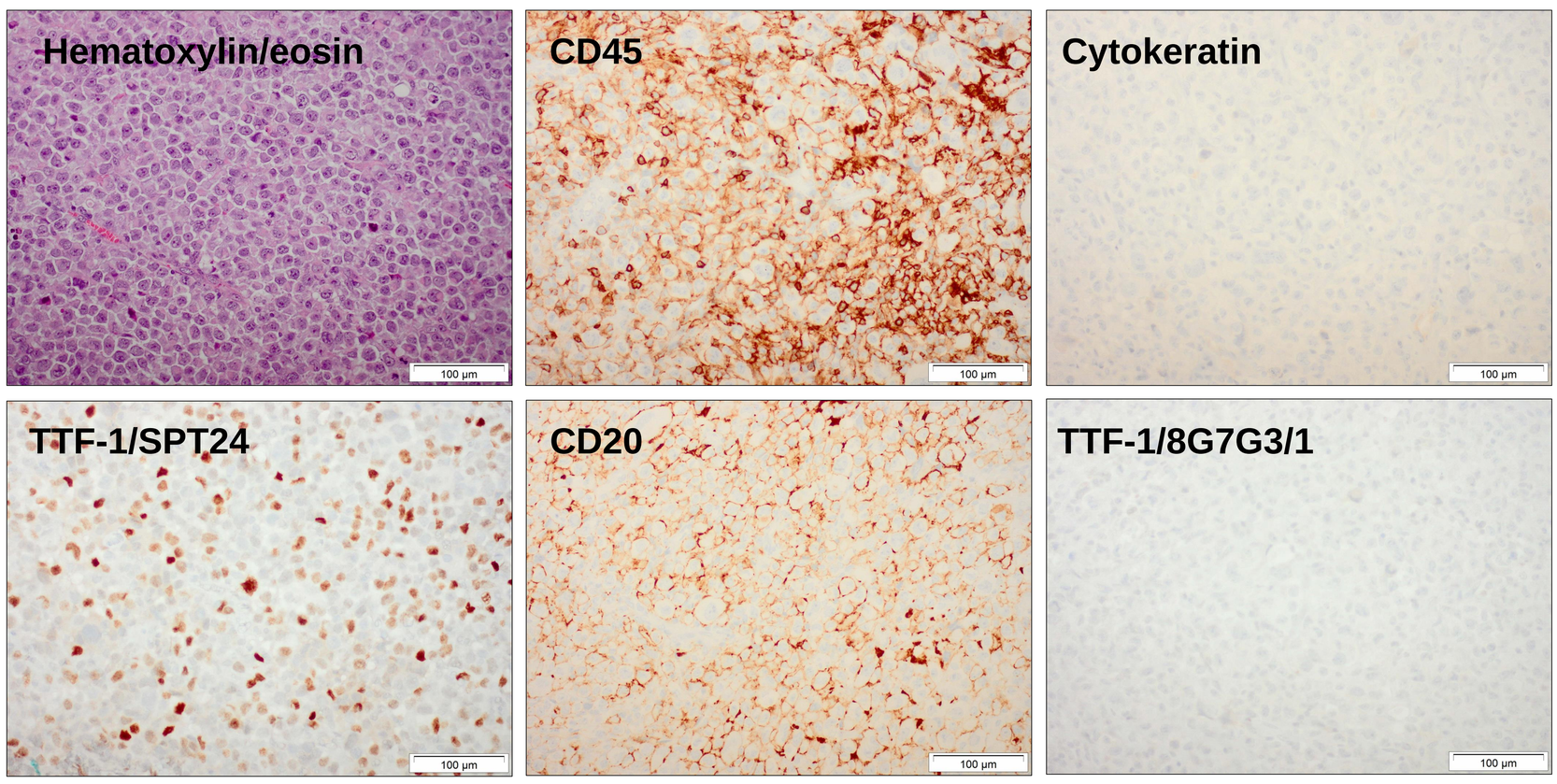
Information on germinal center B-cell-like (GCB) and non-GCB immunohistochemical subgroups based on the Hans algorithm (immunohistochemistry for CD10, Bcl-6 and MUM1) was retrieved from histopathological reports and was available for 93 of 106 cases (88%).

## Index case

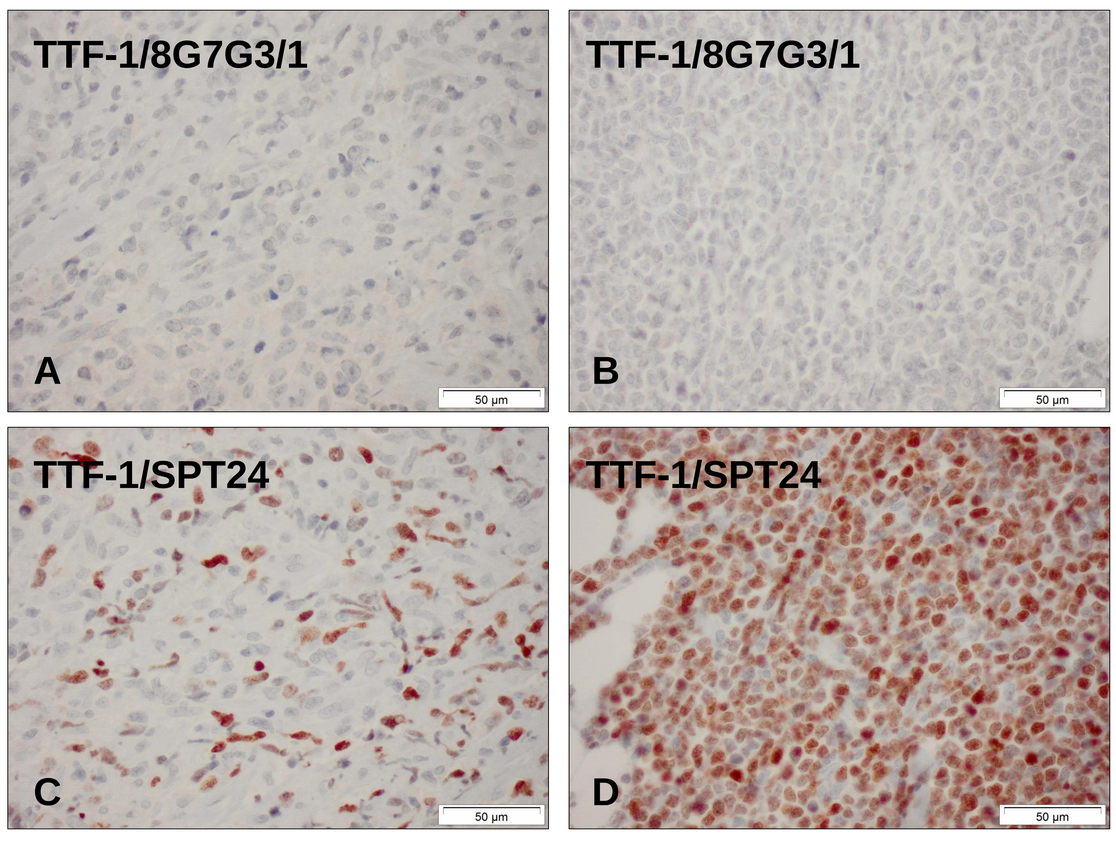
A man with a history of pulmonary adenocarcinoma presented with a subcutaneous mass on the thoracic wall. Routine hematoxylin/eosin staining showed a poorly differentiated large cell neoplasm.

Initial immunohistochemistry showed a lesion which was broad spectrum cytokeratin negative, S100 negative, and CD45 positive. Although the positivity for CD45 indicated a lymphoma, this lesion presented TTF-1/SPT24 expression as well. Additional staining with the 8G7G3/1 clone for TTF-1 was negative.

Further immunohistochemical analysis showed a diffuse large B-cell lymphoma, non-GCB type, with double expression of c-Myc and Bcl-2 without rearrangement of *MYC* and *BCL2* genes.




## TTF-1 expression in a cohort of 105 DLBCL




Immunohistochemical analysis of 105 additional DLBCL cases revealed nuclear staining for TTF-1/SPT24 in 3 extra DLBCL cases (Figures C-D). No nuclear staining for TTF-1/G87G3/1 was observed (Figures A-B). None of the cases presented with cytoplasmic positivity for either of the TTF-1 clones.

In all, this cohort of 106 DLBCL contained 4 cases (3,8%) with nuclear positivity for TTF-1/SPT4. According to the Hans algorithm, two of these DLBCL cases belonged to the germinal center B-cell-like (GCB) immunohistochemical subgroup and two were non-GCB type.

***Figures A and B show no immunohistochemical staining for TTF-1 with the 8G7G3/1 clone in 2 DLBCL cases, whereas figures C and D (same cases) clearly present nuclear staining with the TTF-1/SPT24 clone.***

## Conclusion

Both the 8G7G3/1 and SPT24 clones for TTF-1 are widely used, but our study shows that the SPT24 clone might result in false positive TTF-1 expression in 3,8% of DLBCL. Although this is a rather rare phenomenon, it could present an important diagnostic pitfall during the investigation of a poorly differentiated malignancy. To increase awareness, we recommend that this phenomenon should be included in the datasheet of the Novocastra™ liquid mouse monoclonal SPT24 antibody (Leica Biosystems Newcastle, UK).

**Contact : alessandra.camboni@uclouvain.be and mieke.vanbockstal@ugent.be**