

# Repeatability and reproducibility of qFibrosis for automated assessment of liver fibrosis

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## INTRODUCTION

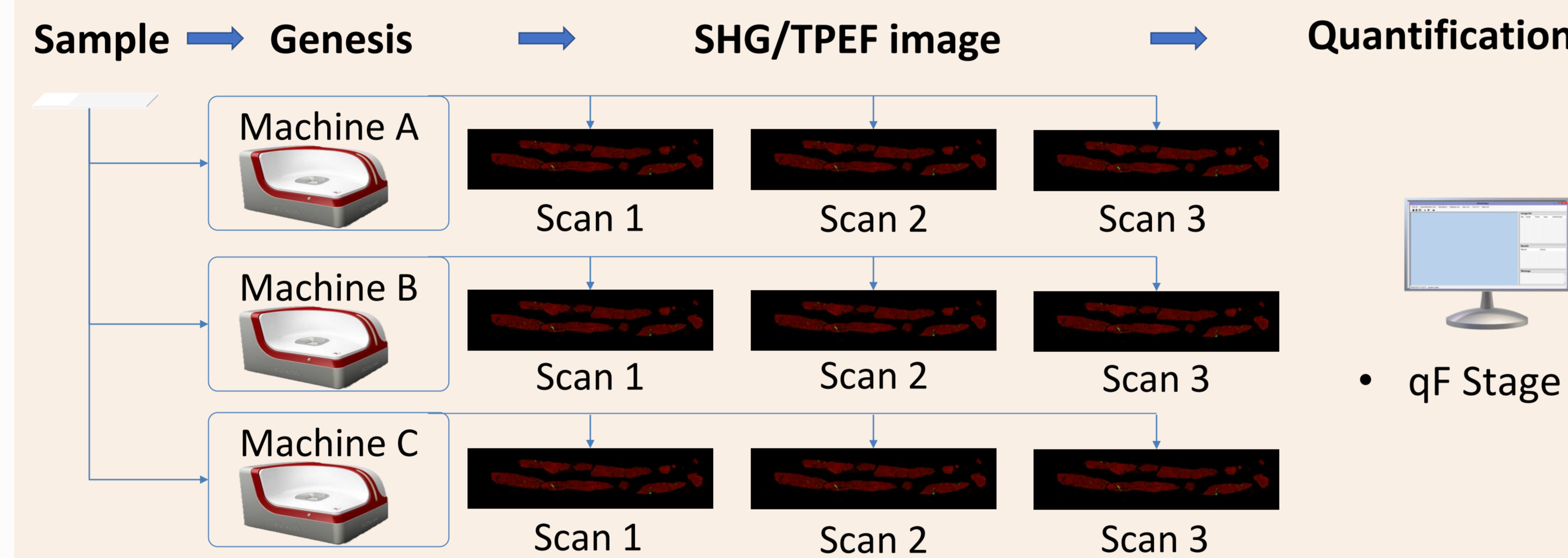
- Fibrosis reduction is a primary endpoint for most non-alcoholic steatohepatitis (NASH) clinical trials, but the inter-/intra observer correlation for fibrosis evaluation is suboptimal based on conventional staging systems.
- The application of digital pathology has gained increased attention in recent years. qFibrosis is an artificial intelligence (AI)-based system for quantifying fibrosis features from liver biopsies and has shown great promise in studies on fibrosis regression/progression and prognosis in NASH.
- In this study, we aim to evaluate the repeatability and reproducibility of the qFibrosis system.

## MATERIALS AND METHODS

- 41 needle biopsy samples of NASH, containing 9, 9, 13 and 10 samples with fibrosis F1, F2, F3 and F4, respectively, were included.
- The second harmonic generation/two-photon excitation fluorescence (SHG/TPEF) images were acquired by 3 Genesis<sup>®</sup> machines. Each sample was scanned 3 times by each machine at different time points.
- qFibrosis stage was calculated by an AI-based algorithm which was previously correlated with NASH Clinical Research Network (NASH CRN) fibrosis staging system.
- Intra-/inter system agreements for qFibrosis stage were calculated to assess the repeatability and reproducibility of the qFibrosis system.

## RESULTS

**Fig.1 Flow chart of the scanning and quantification process. Each sample was scanned 3 times by the same machine at different time-points and was scanned by 3 different machines**

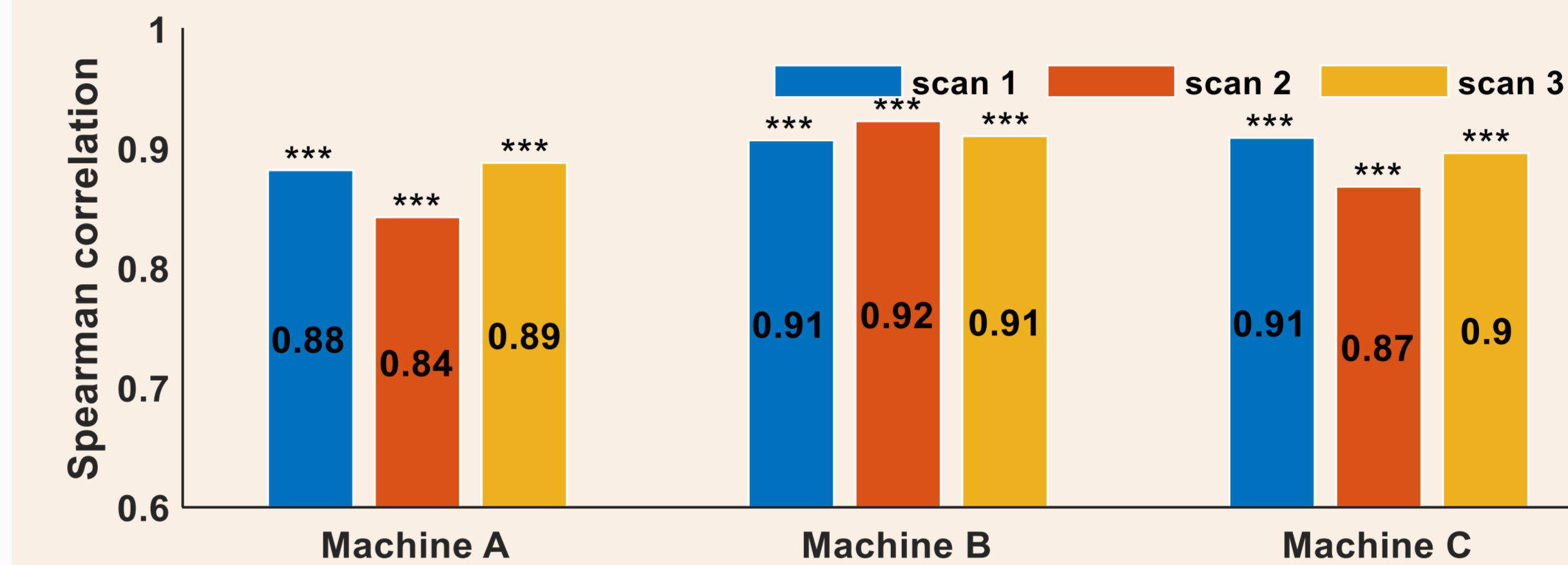


- The Spearman's correlation of qFibrosis stage to NASH CRN fibrosis stage was 0.84-0.92 ( $p < 0.001$ ).
- Inter-observer weighted kappa coefficients for NASH CRN fibrosis staging system were 0.383-0.592 and intra-observer weighted kappa coefficients were 0.679-0.876 reported in the previous study (Beth et al., 2012). The mean intra-/inter system weighted kappa coefficients for qFibrosis stage were greater than 0.83.
- The mean intra-/inter agreements of qFibrosis stage are greater than 85%. Intra-system agreements of the three independent machines are 90%, 90% and 87%, and inter-agreements among the machines are 85%, 86% and 89%, respectively.

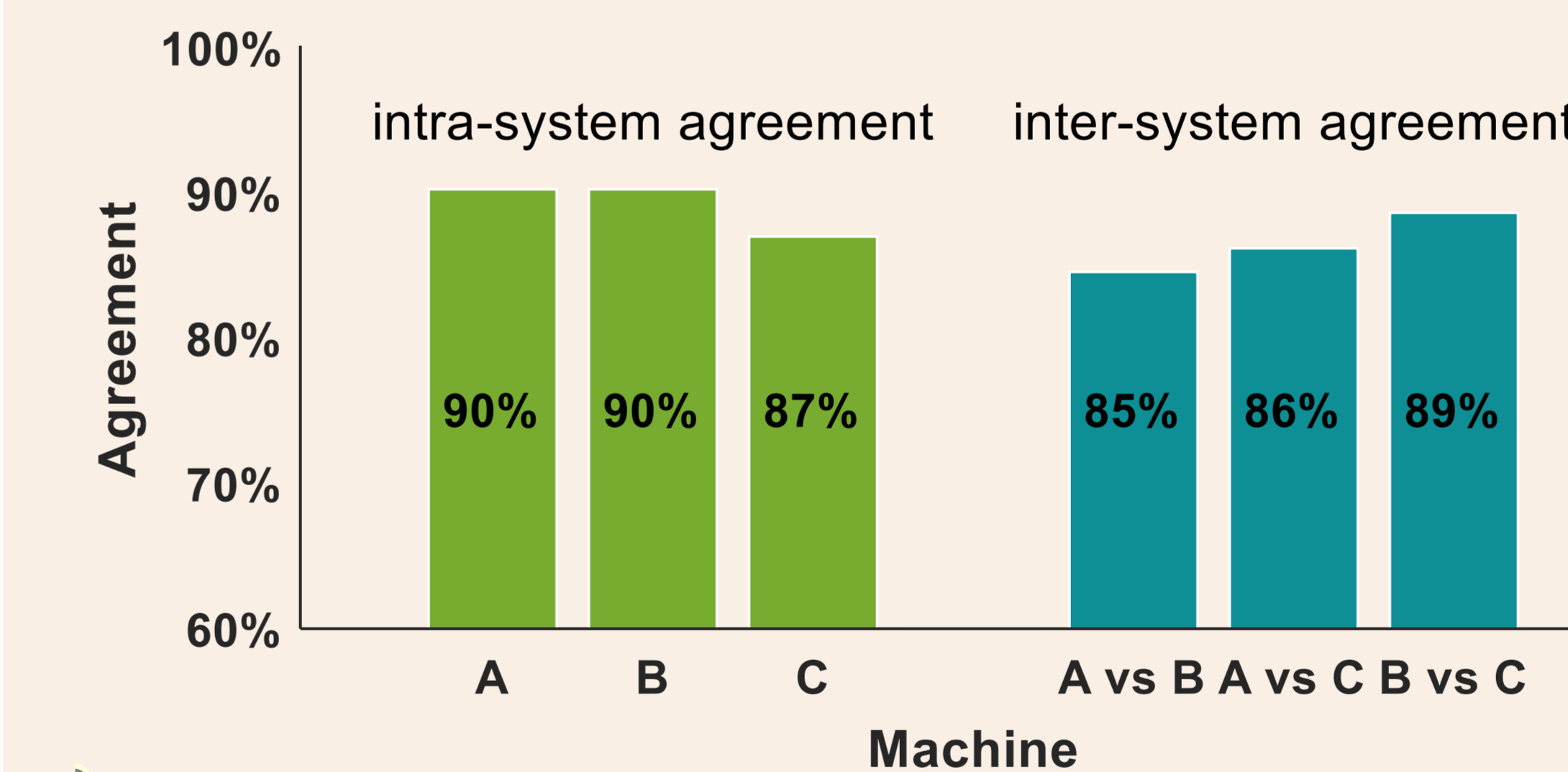
**Table 1. The mean intra-/inter system weighted kappa coefficients for qFibrosis stage**

Inter	Machine A vs B	Machine A vs C	Machine B vs C	Intra	Machine A	Machine B	Machine C
Scan1	0.83	0.86	0.87	Scan 1 vs 2	0.88	0.87	0.84
Scan2	0.81	0.81	0.90	Scan 1 vs 3	0.88	0.85	0.95
Scan3	0.84	0.86	0.87	Scan 2 vs 3	0.88	0.98	0.79
Average	0.83	0.84	0.88	Average	0.88	0.90	0.86

**Fig.2 Spearman correlation of qFibrosis stage to NASH CRN fibrosis stage ( $p < 0.001$ : \*\*\*)**



**Fig.3 The mean intra-/inter-system agreements of qFibrosis stage**



## CONCLUSION

- The qFibrosis system has good repeatability and reproducibility for fibrosis staging. It can provide an accurate reference for pathologists to stage liver fibrosis more objectively for fibrosis progression/regression and anti-fibrotic studies.

## DISCLOSURES

Dr. Arun J. Sanyal declares the following financial interests within the last 24 months: he is president of Sanyal Biotechnology, Stock shareholder of Genfit, Exhalenz, Tiziana, Indalo, NorthSea, Durect, HemoShear, Rivus, Consulting of AstraZeneca, Amgen, Salix, Janssen, Filead, Mallinckrodt, Terns, Merck, Siemens, 89bio, NGM Bio, Poxel, Boehringer Ingelheim, Lilly, HemoShear, Bristol Myers Squibb, Novartis, Novo Nordisk, Pfizer, Albireo, Regeneron, Genentech, Alnylam, Roche, Madrigal, Inventiva, Covance, ProSciento, HistoIndex, PathAI, Genfit, Intercept, Fractyl, Gilead, Grant/Research Support for Gilead, Bristol Myers Squibb, Lilly, Merck, Boehringer Ingelheim, Novo Nordisk, Fractyl, Mallinckrodt, Madrigal, Inventiva, Novartis, royalties of Elsevier, UpToDate.

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