

do not observe, in an underpowered study, a pattern of mutual exclusivity between *NFKBIA* deletion and *EGFR* amplification when analyzing together grades II, III, and IV gliomas, nor do they find a relationship between survival and having a tumor that bears an *NFKBIA* deletion. Since the publication of our report, we have gone on to test these associations with the use of extended data from the Cancer Genome Atlas (TCGA) project. Using gene copy-number data generated by two independent TCGA Genome Characterization Centers on different genotyping platforms, we again observed a pattern of relative mutual exclusivity between deletion of *NFKBIA* and amplification of *EGFR* in glioblastomas ( $P=2\times 10^{-3}$  by Pearson's chi-square test; odds ratio for concomitant deletion and amplification, 0.46; 95% confidence interval [CI], 0.29 to 0.74) (Fig. 1A in the Supplementary Appendix, available with the full text of this letter at [NEJM.org](http://NEJM.org)). We also again observed that patients with tumors with the *NFKBIA* deletion had poorer outcomes than did those who had glioblastomas with normal gene dosages of *NFKBIA* and *EGFR* (hazard ratio for death with the *NFKBIA* deletion, as compared with normal dosages of both *NFKBIA* and *EGFR*, 1.41; 95% CI, 1.02 to 1.94;  $P=0.039$  by the Cox model), and had outcomes

similar to those with tumors harboring *EGFR* amplification (hazard ratio for death with isolated *NFKBIA* deletion, as compared with isolated *EGFR* amplification, 0.93; 95% CI, 0.68 to 1.29;  $P=0.68$  by the Cox model) (Fig. 1B in the Supplementary Appendix). The estimated median survival times were 47 weeks for patients whose tumors harbored an isolated *NFKBIA* deletion, 53 weeks for those whose tumors had isolated *EGFR* amplification, and 67 weeks for those whose tumors had normal dosages of both *NFKBIA* and *EGFR*.

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Since publication of their article, the authors report no further potential conflict of interest.

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## The Hemostatic System as a Modulator of Atherosclerosis

**TO THE EDITOR:** In their review article (May 5 issue),<sup>1</sup> Borisoff et al. describe the role of hemostatic mechanisms as potential modulators of atherosclerotic plaque phenotype. Although they describe the role of thrombin as a critical mediator in the processes of coagulation, inflammation, and maintenance of vessel walls and even as an anticoagulant molecule, they provide no information regarding the contribution of the thrombin-activatable fibrinolysis inhibitor (TAFI) in these processes. TAFI is a procarboxypeptidase that on activation by thrombin or thrombin-thrombomodulin turns into a potent antifibrinolytic enzyme. TAFI acts as a molecular link between the processes of coagulation and fibrinolysis. Excessive TAFI levels can foster thrombosis by inducing a hypofibrinolytic state. In fact, plasma levels of TAFI are increased in patients with stroke and correlate with stroke severity in some studies.<sup>2-4</sup> In addition, TAFI significantly affected the effi-

cacy of recombinant tissue plasminogen activator and vessel recanalization in patients undergoing thrombolysis after acute ischemic stroke.<sup>5</sup> Because of the prominent role of thrombin in atherosclerosis, as stated by Borisoff et al., I believe that TAFI, a potent fibrinolytic inhibitor mediated by thrombin, should be included in discussions of the complex interplay between hemostasis and atherosclerosis.

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**THE AUTHORS REPLY:** We concur with Páramo that beyond modulating the ultimate clot size and lysis, the fibrinolytic cascade proteins (including TAFI<sup>1</sup>) may also contribute to the pathophysiology of cardiovascular disease. Nevertheless, the exact role of fibrinolysis in atherosclerosis remains highly controversial to date. Owing to space limitations, we restricted the scope of the review and did not cover this topic.

Hypofibrinolysis has been proposed as a determinant of cardiovascular disease in previous studies.<sup>2</sup> Aside from their recognized effects on fibrin clot lysis, fibrinolytic proteins, including the enzyme plasmin, should be recognized for their involvement in regulating many other actions, such as the plasmin-mediated accelerated inflammation and degradation of matrix proteins. Plasmin activates distinct matrix metalloproteinases (MMPs), such as MMP-3, 9, 12, and 13,<sup>3</sup> which have contributed to enhanced elastolysis and collagenolysis, tunica media destruction, and aneurysm formation in atherosclerotic mice

models.<sup>4</sup> Furthermore, despite the atheroprotective effect of plasminogen and urokinase-type plasminogen activator, the loss of plasminogen activator inhibitor 1 in atherosclerotic mice has been paradoxically linked to increased plaque growth and extracellular matrix deposition.<sup>5</sup> Hence, the net effects of a fibrinolytic imbalance between plasminogen activators and their inhibitors on atherosclerosis progression remain poorly understood.

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Since publication of their article, the authors report no further potential conflict of interest.

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## In Vivo Biomechanical Measurements of a Football Player's C6 Spine Fracture

**TO THE EDITOR:** During an investigation of concussion in American football players, we captured in vivo biomechanical data on a cervical spine fracture as it occurred in a male athlete (age, 18 years; height, 189.0 cm; weight, 79.4 kg) who was performing a head-down tackling maneuver. The cornerback's helmet was equipped with the Head Impact Telemetry System (Simbex), a six-accelerometer array that measures the location and magnitude of an impact. The impact magnitude was quantified by measuring peak linear and rotational acceleration of the head with the use of the Gadd Severity Index (GSI) and

Head Injury Criteria (HIC).<sup>1,2</sup> The GSI and HIC are mathematically weighted measures of head acceleration and the duration of impact, with higher scores representing increased likelihood of injury.

After being transported to the emergency department, the athlete reported having pain in the head, neck, and lower back (severity between 3 and 5 on a scale of 0 through 10, with 0 indicating no pain and 10 indicating most severe pain) and losing consciousness for less than 10 seconds at the time of injury. A computed tomographic (CT) scan of the brain was normal, but