Telomerase activity and loss of chr10p in gliomas

Leuraud et al. show that chromosome 10p deletions and telomerase activity, two frequent features in malignant gliomas, are tightly related, supporting the specific inactivation of a putative telomerase repressor gene on 10p15.1.

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Commentary by Lisa DeAngelis, MD

All cancers, including gliomas, arise from a series of genetic changes that stimulate uncontrolled cell growth and permit the cell to avoid apoptosis. Another mechanism, common to many cancers, leads to immortalization because of persistent activity of telomerase, an enzyme that stabilizes telomeric length, preventing normal cell senescence and thus permitting continued cell proliferation.¹ In this issue, Leuraud et al. investigate the incidence and mechanism of telomerase activity in malignant gliomas. Recognizing the frequent loss of chromosome 10 in malignant gliomas, they investigated the relationship between loss of heterozygosity (LOH) of chromosome 10 and telomerase activity because of the recent identification of a telomerase repressor mapped to 10p. The authors identified telomerase activity in 55% of malignant gliomas tested and this was strongly correlated with 10p LOH, suggesting that loss of the 10p repressor may be responsible for per-

A case which displays telomerase activity, as shown by the TRAPeze Telomerase Detection Kit (Serologicla Corporation, Norcross, GA), allele 1 of D10S249 has been lost (LOH = loss of heterozygosity).

sistent telomerase activity in these tumors.

Telomerase activity was usually associated with 10p LOH, but three tumors with an intact chromosome 10 also had detectable telomerase, and 45% of tumors, some with chromosome 10 LOH, had no telomerase. These findings underscore the various and complex changes that can

lead to glial neoplasms. Heterogeneity is seen not only among gliomas but also within the tumor of an individual patient.^{2,3} This intratumoral variability is difficult to identify and makes single targeted or genetic therapy unlikely to succeed. Consequently, there will be no easy therapeutic solutions to the glioblastoma, and definitive treatment will probably require that multiple targets be attacked simultaneously.

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Striatal activation during benign essential blepharospasm (BEB)

Activation of right putamen.

Schmidt et al. obtained fMRI in six patients with BEB. Blinking in healthy control subjects or patients with BEB produced variable activation of cerebellum, visual, and sensorimotor areas, whereas activation of the putamen consistently correlated with epochs of eyelid spasms only in the patients with BEB but not with blinking in the control subjects.

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The accompanying editorial by Evinger and Perlmutter notes that current views of BEB propose that BEB is caused by the interaction of a genetic predisposition with environmental triggers such as dry eyes, changing basal ganglia pathways. While noting that many areas of brain are involved in blinking, so that abnormalities may be detected wherever one looks, Evinger and Perlmutter highlight the fact that this study focused on findings specific to abnormal blinking and suggest that putamen function is critical in BEB.

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Levodopa learning and hallucinations in PD

Feigin et al. studied motor sequence learning with PET in PD. Levodopa impaired learning; this was accompanied by enhanced activation in right premotor cortex and a decline in activation of the ipsilateral occipital association area. Levodopa-induced changes in occipital association cortex correlated with learning indices. The authors speculate that these changes may be the basis for the visual hallucinosis that can be produced by dopaminergic therapy.

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Pharmacogenetic predictors of adverse effects of L-dopa

Kaiser et al. investigated whether polymorphisms in the dopamine receptor and transporter genes (*DAT*) are predictors of adverse effects of L-dopa in patients with PD. They found an association between a polymorphism of the *DAT* and the occurrence of psychosis or dyskinesia.

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Dietary iron and manganese and PD risk

In an epidemiologic case-control study, Powers et al. observed a nearly twofold increase in risk for idiopathic PD in persons who typically consumed diets with relatively high levels of iron and manganese, relative to diets with lower levels of both.

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Stroke associated with IVIg administration

Caress et al. describe 16 cases of stroke following IVIg infusion. Almost 90% of the cases occurred within 24 hours and half were in patients receiving their first course of therapy.

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tPA for arterial thrombosis induced by IVIg

Okuda et al. report arterial thrombosis as the cause of stroke following IVIg in four patients with no evident antecedent atherosclerosis. Stroke resolved with tPA treatment.

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The accompanying editorial by Dalakas and Clark summarizes the neurologic uses of IVIg and potential mechanisms and the few severe but rare complications: anaphylaxis, renal tubular necrosis, and, as in the Caress et al. and Okuda et al. reports, thrombosis events. They consider the mechanism of stroke and speculate that strategies to reduce vascular risk factors might reduce the likelihood of stroke.

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Prism adaptation treatment of neglect: Conflicting results?

Facial chimera.

In contrast, Ferber et al. explored the effects of prism adaptation on spatial neglect using chimeric face stimuli (half-smiling, half-neutral faces). Whereas prism treatment improved exploratory eye movements into contralesional space, they failed to alter the impaired awareness of stimuli in left space.

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Maravita et al. showed that prism adaptation effectively improved not only visual neglect, but also extinction, suggesting that this treatment influences both exploration and attention.

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The accompanying editorial by Beversdorf and Heilman discusses some of the mechanisms of spatial neglect and extinction as well as the means by which prism adaptation might improve these disorders. The editorial also attempts to reconcile the contradictory results of these two studies by explaining that there are multiple tests for neglect and several forms of neglect. Thus, the difference in results between these two studies suggests that prism adaptation is not a neglect syndrome panacea and the difference between studies might have been related to subject or test selection.

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Serial paintings from an artist with simultanagnosia

Smith et al. studied an artist with a top-of-the-basilar artery stroke who painted weekly following her stroke. Analysis of her paintings provides insight into the internal representation of visual memory in a patient with simultanagnosia.

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Modulation of time perception induced by rTMS

In this article, Koch et al. demonstrate that it was possible to modulate subjective time perception by transiently reducing the excitability of the right dorsolateral prefrontal cortex in normal humans.

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