

Image Improvement from a Sodium-Layer Laser Guide Star Adaptive Optics System

C. E. Max,* S. S. Olivier, H. W. Friedman, J. An, K. Avicola, B. V. Beeman, H. D. Bissinger, J. M. Brase, G. V. Erbert, D. T. Gavel, K. Kanz, M. C. Liu, B. Macintosh, K. P. Neeb, J. Patience, K. E. Waltjen

A sodium-layer laser guide star beacon with high-order adaptive optics at Lick Observatory (Mount Hamilton, California) produced a factor of 2.4 intensity increase and a factor of 2 decrease in full width at half maximum for an astronomical point source, compared with image motion compensation alone. The image full widths at half maximum were identical for laser and natural guide stars (0.3 arc second). The Strehl ratio with the laser guide star was 65 percent of that with a natural guide star. This technique should allow ground-based telescopes to attain the diffraction limit, by correcting for atmospheric distortions.

Images of astronomical objects are distorted by variations in the index of refraction of air due to atmospheric turbulence. These aberrations limit the resolution [for example, the full width at half maximum (FWHM)] of long-exposure images to ~ 0.5 arc sec at visible and near-infrared (IR) wavelengths. If the effects of turbulence could be fully corrected, telescopes with diameters of 1 to 10 m would achieve resolutions of 0.1 to 0.01 arc sec at a $0.5\text{-}\mu\text{m}$ wavelength. Adaptive optics systems that sense and correct atmospheric aberrations were proposed by Babcock in 1953 (1). About 10 such systems are now installed on astronomical telescopes (2), including one developed for the 3-m Shane Telescope at Lick Observatory (3). These systems use a natural star as a reference beacon. However, requirements on reference beacon brightness and proximity typically restrict the use of natural guide star adaptive optics systems to a small fraction ($<10\%$) of the sky.

In principle, laser guide star systems can create reference beacons anywhere in the sky. Two techniques to generate the laser beacon are being pursued. The first uses Rayleigh scattering from air molecules at altitudes of 10 to 15 km. A system using this technique is in operation on a 1.5-m telescope at the Starfire Optical Range (4). Because Rayleigh scattering is limited to $<15\text{-km}$ height by the exponential decrease in air density, the wave front from a Ray-

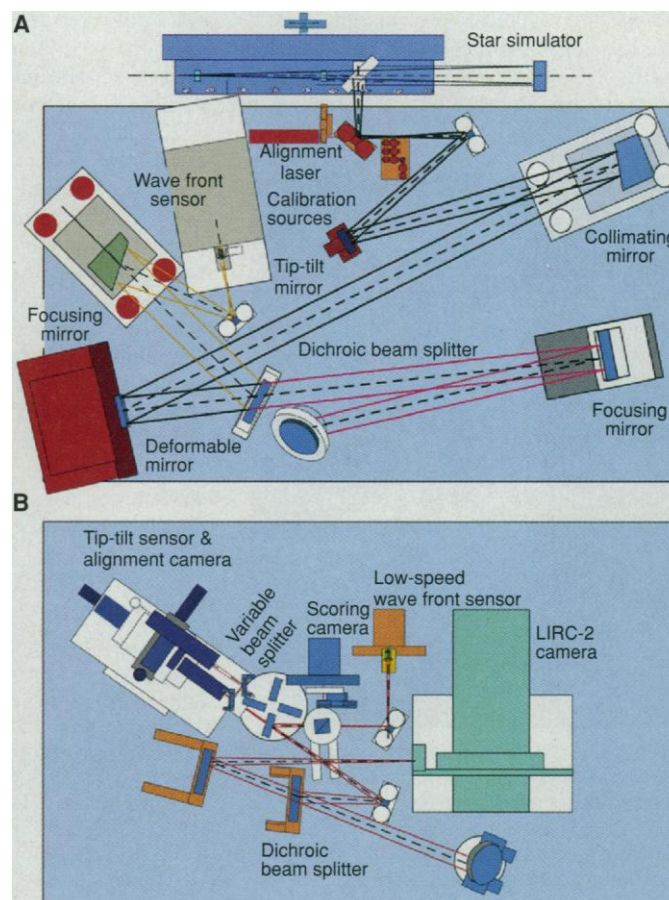
leigh beacon does not sample the same aberrations as the wave front from an astronomical object. This is called the cone effect because the Rayleigh beacon samples a

cone instead of a cylinder. The cone effect, also known as focus anisoplanatism (5), is more pronounced for a lower altitude reference beacon and for a larger telescope. For telescopes with diameters of 6 to 10 m, the cone effect from a Rayleigh beacon limits the ability to correct for atmospheric turbulence.

The second technique is the use of laser-produced resonance fluorescence of atomic Na in the mesosphere at a height of ~ 95 km (laser wavelength of 589 nm corresponding to the sodium D_2 line) (6, 7). The 95-km height of the sodium layer reduces the cone effect, compared with a Rayleigh beacon. Passive high-order (8) and low-order (9) wave front phase measurements that use a sodium-layer laser guide star have been performed. Active image improvement that uses a sodium-layer laser guide star with a low-order, image-stacking system on the Multiple Mirror Telescope was accomplished in 1994 (10). Here, we report image improvement with a high-order adaptive optics system and a sodium-layer

Fig. 1. Lick adaptive optics system schematic.

(A) Front view. Light from the telescope enters from top center on the diagram and hits two turning mirrors, the tip-tilt mirror, an off-axis parabolic collimating mirror, and the deformable mirror. The light then hits a dichroic beam splitter that reflects wavelengths shorter than 600 nm to the wave front sensor leg consisting of an off-axis parabolic focusing mirror, a turning mirror, a collimating lens, the lenslet array, a set of relay telescope lenses, and finally the wave front sensor camera. Light at wavelengths longer than 600 nm passes through the dichroic beam splitter to the science camera leg, consisting of an off-axis parabolic focusing mirror, a turning mirror, a collimating lens, the lenslet array, a set of relay telescope lenses, and finally the wave front sensor camera. (B) Rear view. A turning mirror receives the light from the front side of the optical bench, and a dichroic beam splitter transmits wavelengths longer than 900 nm to a turning mirror and then to an IR science camera, LIRC-2. Wavelengths shorter than 900 nm are reflected from the dichroic beam splitter to a turning mirror. A variable beam splitter after the turning mirror passes a selectable fraction of the light to the tip-tilt sensor and reflects the rest to a beam splitter cube. Half the light from this cube goes to a CCD scoring camera, and the other half goes to a low-speed wave front sensor. The latter is used to monitor focus and other slowly varying aberrations introduced by the laser guide star.



C. E. Max, S. S. Olivier, H. W. Friedman, J. An, K. Avicola, B. V. Beeman, H. D. Bissinger, J. M. Brase, G. V. Erbert, D. T. Gavel, K. Kanz, B. Macintosh, K. P. Neeb, K. E. Waltjen, Lawrence Livermore National Laboratory, 7000 East Avenue, Livermore, CA 94550, USA. M. C. Liu, Department of Astronomy, University of California, Berkeley, CA 94720, USA. J. Patience, Department of Physics and Astronomy, University of California, 405 Hilgard Avenue, Los Angeles, CA 90024, USA.

*To whom correspondence should be addressed.

laser guide star.

The Lick Observatory adaptive optics system (3) is mounted at the $f/17$ Cassegrain focus (the f number is a measure of image brightness) of the 3-m Shane Telescope (11). The adaptive optics system (Fig. 1) feeds LIRC-2, a near-IR camera based on a HgCdTe 256 by 256 pixel detector. The deformable mirror corrects the wave front phase over the telescope pupil. This thin glass mirror has 127 electro-restrictive (lead magnesium niobate) actuators in a triangular pattern, each capable of deforming the front surface by up to ± 4 mm; 61 of the actuators are actively controlled. A separate, flat, fast-steering mirror is used to correct the overall wave front tip-tilt (image motion). The Shack-Hartmann wave front sensor (12) has 37 subapertures in the clear aperture of the telescope (a subaperture diameter of 44 cm mapped to the primary mirror). The wave front sensor uses a 64 by 64 pixel charged-coupled device (CCD), with read noise of 7 electrons per pixel at 1200 frames s^{-1} . In laser guide star mode, a separate sensor is used for tip-tilt (13, 14), with four photon-counting avalanche photo-diodes configured as a quad cell. A dedicated analog controller uses input from this tip-tilt sensor to control the fast-steering mirror in the adaptive optics system, at a

bandwidth of up to 120 Hz.

The wave front control computer is a 160-Mflop Mercury system with four Intel i860 processors. It is operated at a sample rate of up to 500 Hz with a control bandwidth (0-dB crossover) of up to 30 Hz, including camera integration and readout rate, compute rate, and transfer rate to the deformable mirror drivers. In the laser guide star mode, the average wave front sensor tip-tilt is used by a separate digital processor to control a high-bandwidth steering mirror within the laser launch optics, stabilizing the laser guide star on the wave front sensor.

The laser guide star (15) is a tunable dye laser pumped by flash-lamp-pumped, frequency-doubled Nd:yttrium-aluminum-garnet (YAG) lasers. Pump lasers are located in a room below the telescope dome and are fiber-optically coupled to the dye laser on the side of the 3-m telescope (Fig. 2). The dye laser produces light tuned to 589 nm, which is projected into the sky by a refractive launch telescope with a 30-cm primary lens (16). The laser projects 18 W of average power with a pulse width of ~ 100 ns and a pulse repetition rate of ~ 11 kHz.

In our experiments of September to October 1996, the measured value of the atmospheric coherence length r_0 was ~ 11 cm at 0.55 μm . The apparent size of the guide star in the sodium layer was measured in 10-s exposures and was found to be ~ 2 arc sec. The return signal from the laser guide star was comparable with that for a natural star with a magnitude of 7.0 in the V band ($\lambda = 5550 \text{ \AA}$ and $\Delta\lambda \sim 1000 \text{ \AA}$). This return signal was a factor of 2 higher than that measured at Lawrence Livermore National Laboratory (LLNL) in 1992 (8) for comparable laser power and a factor of ~ 4

higher than previous measurements at Lick. Factor of 2 to 4 changes in return flux were expected because of seasonal and night-to-night variation in sodium column density.

The field stars γ Trianguli and SAO 56102 were observed with the IR camera at exposure times of 20 and 60 s, respectively (Fig. 3). Compared with tip-tilt correction alone, laser guide star adaptive optics increased the peak intensity by a factor of 2.4 and decreased its FWHM by a factor of 2. Relative to the uncorrected images, peak intensity was increased by a factor of 1.4 for tip-tilt correction alone (17), by 4.2 for tip-tilt with natural guide star adaptive optics, and by 3.3 for tip-tilt with laser guide star adaptive optics. The FWHM was decreased by a factor of 1.3 (from 0.8 to 0.6 arc sec) for tip-tilt correction alone and by a factor of 2.7 (to 0.3 arc sec) for natural and laser guide star correction. Both the laser guide star and the field star were on-axis. Light from the field star was attenuated on the wave front sensor with the use of a narrowband filter centered at 589 nm. The field star was used as the tip-tilt guide star. Images (Fig. 3) were made at about 5° from zenith with sampling frequency of 200 Hz. Similar image improvement was obtained on 30 September and 1 October as well as on 26 and 27 November 1996, the latter observations under seeing conditions that were worse than those of 30 September and 1 October by a factor of 2 to 3 with 30 to 40 mph surface winds. All nights showed little temperature variation; correction for primary mirror-aberrations was small. The increase in peak intensity with laser guide star adaptive optics was 75% of the increase for natural guide stars, with all other system parameters (including tip-tilt) held constant. The corrected FWHM was identical

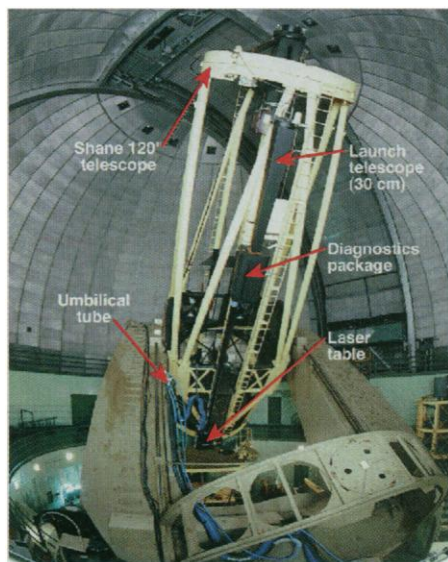
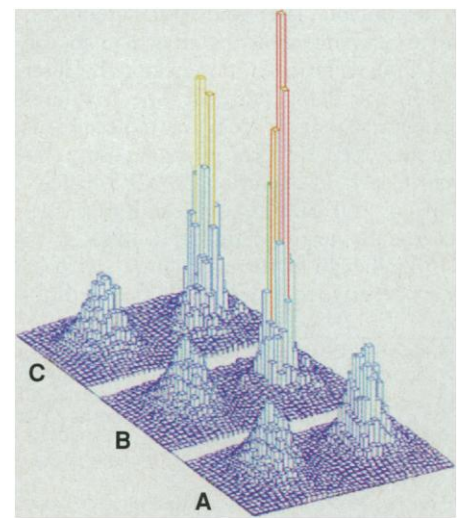


Fig. 2. The LLNL laser guide star installation at Lick Observatory. The dye master oscillator and the Nd:YAG pump lasers are in a room below the dome floor. An umbilical tube from this room to the telescope contains the lines that carry the dye, as well as optical fibers carrying high-power green YAG light and low-power yellow light from the dye master oscillator to the dye laser amplifier on the telescope. High-power yellow light from the dye laser amplifier travels up through the diagnostics package that monitors beam pointing and wave front quality and propagates into the sky through the launch telescope.

Fig. 3. Image data without (left) and with (right) correction using (A) the tip-tilt system alone, (B) both the tip-tilt and high-order adaptive optics systems with a natural guide star, and (C) both the tip-tilt and high-order adaptive optics systems with the sodium-layer laser guide star. These images of the field stars γ Trianguli [(A) and (B)] (20-s exposures) and SAO 56102 (C) (60-s exposures) were recorded within an hour on 1 October 1996 at a wavelength of 2.2 μm . The image peak intensities after correction by adaptive optics were 1.4 (A), 4.2 (B), and 3.3 (C) times the respective uncorrected values. The corrected image widths were 0.6 (A) and 0.3 arc sec [(B) and (C)], a factor of 1.3 (A) and 2.7 [(B) and (C)], respectively, less than the uncorrected size of 0.8 arc sec. The increase in peak intensity when the laser guide star was used was 75% of that when the natural guide star was used, with other system parameters (including tip-tilt) held constant. [The uncorrected image for γ Trianguli in (A) and (B) has a normalized peak intensity 18% higher than that for SAO 56102 in (C), because of minor differences in exposure times, calibration, and atmospheric conditions.]



for the laser and natural guide stars.

The power spectrum of wave front phase fluctuations measures the power per unit frequency interval present in residual uncorrected phase aberrations. The open- and closed-loop phase power spectra (Fig. 4) for a natural guide star and a laser guide star are similar. For both systems, adaptive optics decreased residual phase fluctuations at low frequencies, with the correction losing its impact at frequencies greater than 5 to 10 Hz. The noise floor above 10 Hz (Fig. 4) was due to the fact that above a certain frequency, the noise is larger than the signal. The noise floor for the laser guide star was higher than that for the natural guide star, because the laser spot is larger and dimmer.

Strehl is a measure of image quality: the ratio of measured peak intensity to that of a

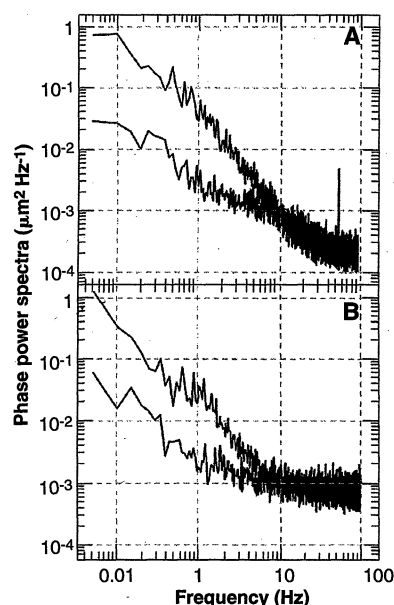


Fig. 4. Reconstructed phase power spectra for (A) the bright natural star, γ Trianguli, and (B) the sodium-layer laser guide star. In each panel, the upper curve was calculated from data taken with the control loop open, and the lower curve was calculated from data taken with the control loop closed (1 October 1996). Laser guide star and natural guide star data were recorded at approximately the same time as the images shown in Fig. 3. Because the Hartmann sensor used 4 by 4 pixels (1.8 arc sec per pixel or 7.2 arc sec width of the quad cell overall) for centroid determination, the dynamic range of the wave front sensor was more than enough to accommodate the open-loop measurements, which showed rms image motion of about 1 arc sec. Each power spectrum was calculated from a series of 4096 wave front sensor centroid measurements at a sampling frequency of 200 Hz. The control bandwidth (0-dB crossover) was ~ 10 Hz. This bandwidth measures the highest speed at which the control loop can correct phase aberrations. Atmospheric coherence time τ_0 was 250 to 500 ms.

theoretical image limited only by diffraction. The Strehl of the laser guide star corrected image was 0.091, 65% of that measured for the natural guide star (Table 1). Ten percent of this difference was due to poorer performance of the tip-tilt system (discussed further below). The remainder was due to differences in size and shape on the wave front sensor between the laser guide star and the natural star and to focus error introduced when the height of the sodium layer was not perfectly sensed.

The Strehl ratio can be decomposed into six contributing sources of residual aberration (18) (Table 1). Fitting error is due to limitations on the ability of the deformable mirror to respond to high-spatial-frequency variations of the atmosphere, because of the finite number of actuators. The fitting error was estimated with the use of a standard scaling law from atmospheric turbulence theory (19) with atmospheric coherence length from the uncorrected image FWHM. Servo error is due to the finite bandwidth of the control loop and was calculated from the integral of the measured phase power spectrum after removal of the noise floor. Measurement error is due to the finite ability of the wave front sensor to measure the wave front in the presence of noise. Measurement error was calculated from the integral of the power spectrum noise floor, taking into account filtering of the noise by the control loop (20). Because the total measurement error was quite small for these experiments, finite laser guide star spot size was not a significant factor (21). Tip-tilt error (servo error plus measurement error) represents the finite ability of the tip-tilt system to stabilize image motion. For the natural guide star, tip-tilt error was calculated from power spectra of wave front sensor centroid positions averaged over the

pupil, after taking into account the intrinsic measurement error of the average centroid position. For the laser guide star, the average centroid position is affected by the deviation of the laser beam as it propagates upward. Tip-tilt measurement error for the laser was calculated by assuming the same servo error as for the natural guide star and scaling the measurement error by the measured decrease in the sum voltage signal on the tip-tilt sensor quad cell. Calibration error was due to residual non-common path aberration between the wave front sensor and science camera focal planes. Cone effect measures the difference between the wave front measured from the finite-altitude laser guide star and from a real star located an "infinite" distance away. When appropriate, the Strehl ratios (Table 1) were approximated by $\exp(-\sigma^2)$, where σ is the root mean square (rms) wave front error in radians at 2.2 μm .

Residual error in calibration of non-common path optics arose from the adaptive optics system and from inside the IR camera dewar. Calibration error for the adaptive optics system was measured with a white-light reference source and a CCD camera with a narrowband filter centered at 700 nm. Calibration error for the IR camera was measured with the white-light source and two different filters within the IR camera. The filter with narrower bandwidth, used for the brighter natural guide star, had slightly more measured error. Calibration error was minimized by adjusting the deformable mirror to produce the best reference image.

For laser and natural guide stars, the measured Strehl was about 0.6 of that predicted from the measured error sources. This Strehl measurement implies that there was a secular drift in calibration over the

Table 1. Residual errors for adaptive optics correction using both a natural and laser guide star.

	Strehl ratio	
	Natural guide star adaptive optics	Laser guide star adaptive optics
Measured Strehl from corrected image	0.14	0.091
Measured Strehl from uncorrected image	0.028	0.028
Predicted or measured Strehl from individual wave front error sources:		
Fitting error	0.82	0.82
Servo error	0.81	0.89
Measurement error	0.98	0.95
Tip-tilt error	0.76	0.66
Calibration errors		
Internal to AO system	0.89	0.89
Internal to IR camera	0.52	0.57
Predicted cone effect	—	0.98
Total predicted Strehl after correction	0.23	0.23
Inferred internal calibration drift	0.6	0.6
Inferred laser guide star calibration error	—	0.65

6-hour interval between the last calibration and the image data collection. The drift was due to flexure from temperature effects and other mechanical stresses, as well as inaccuracies in repositioning the wave front sensor between the focal positions for the natural guide star and the laser star. These errors can be reduced by calibrating more frequently.

NOTES AND REFERENCES

1. H. W. Babcock, *Publ. Astron. Soc. Pac.* **65**, 229 (1953); *Science* **249**, 253 (1990).
2. L. A. Thompson, *Phys. Today* **47**, 24 (1994).
3. J. M. Brase et al., *Proc. Soc. Photo-Opt. Instrum. Eng.* **2201**, 474 (1994); S. S. Olivier et al., *ibid.*, p. 1110.
4. R. Q. Fugate et al., *Nature* **353**, 144 (1991).
5. D. Fried, *J. Opt. Soc. Am. A* **11**, 277 (1994); ——— and J. F. Belsher, *ibid.*, p. 227.
6. W. Happer, G. MacDonald, C. E. Max, F. Dyson, *ibid.*, p. 263.
7. R. Foy and A. Labeyrie, *Astron. Astrophys.* **152**, L29 (1985).
8. K. Avicola et al., *J. Opt. Soc. Am. A* **11**, 825 (1994).
9. R. A. Humphreys, C. A. Primmerman, L. C. Bradley, J. Herrmann, *Opt. Lett.* **16**, 1367 (1991). Measurements of laser guide star centroid motion were made in two contiguous subapertures.
10. M. Lloyd-Hart et al., *Astrophys. J.* **439**, 455 (1995). This system allowed control of relative tip-tilt between two (and, subsequently, all six) of the Multiple Mirror Telescope's 1.8-m primary mirrors.
11. S. S. Olivier et al., *Proc. Soc. Photo-Opt. Instrum. Eng.* **2534**, 26 (1995).
12. A Shack-Hartmann sensor divides the telescope pupil into subapertures with the use of a set of miniature lenses (lenslet array) placed in a reimaged pupil plane. The average wave front slope in each subaperture was determined by measuring the position of the focused image formed by each lenslet. The constraint of continuity could then be imposed, and an estimate of the wave front phase could be reconstructed, for example, from a leastsquares fit.
13. Because the laser travels up through the turbulent atmosphere before forming the guide star, the instantaneous physical position of the guide star is variable. This upgoing beam wander results in a difference between the apparent instantaneous positions of a laser guide star and a natural star, rendering the laser guide star unsuitable as a reference for stabilization of the overall image position of astronomical objects. The solution is to use a faint natural star as overall tip-tilt reference. If this technique is used, the sky coverage for a laser guide star adaptive optics system is limited by the availability of suitable tip-tilt reference stars [S. S. Olivier, C. E. Max, D. Gavel, J. Brase, *Astrophys. J.* **407**, 428 (1993); (14)]. Because the requirements for a tip-tilt reference star are less severe than those for a high-order wave front reference beacon, the use of a laser guide star increases the sky coverage fraction for adaptive optics systems.
14. S. S. Olivier and D. T. Gavel, *J. Opt. Soc. Am. A* **11**, 368 (1994).
15. H. Friedman et al., *Proc. Soc. Photo-Opt. Instrum. Eng.* **2201**, 352 (1994); H. W. Friedman et al., *ibid.* **2534**, 150 (1995).
16. H. W. Friedman et al., in *Proceedings of the European Southern Observatory, Conference No. 54* (European Southern Observatory, Garching, Germany, 1995), p. 207–211.
17. For the measured seeing conditions (0.8 arc sec at $\lambda = 2.2 \mu\text{m}$ and $r_0 = 10.7 \text{ cm}$ at $\lambda = 0.55 \mu\text{m}$), direct integration of the modulation transfer function for telescope and ensemble-averaged atmosphere [D. L. Fried, *J. Opt. Soc. Am.* **56**, 1372 (1966); D. T. Gavel and S. S. Olivier, *Proc. Soc. Photo-Opt. Instrum. Eng.* **2201**, 295 (1994)] showed that the expected increase in peak intensity for tip-tilt correction was a factor of 3.7. However, taking into account the measured and inferred calibration errors of 1.7 rad^2 (assuming that

they have roughly the same spectrum as the tilt-corrected atmosphere), the expected intensity increase was only a factor of 1.7. The measured value was 1.4. The degraded tip-tilt performance was attributable to misalignment of the tip-tilt sensor and nonoptimal tuning of the tip-tilt control parameters.

18. For a review, see J. M. Beckers, *Annu. Rev. Astron. Astrophys.* **31**, 13 (1993).
19. D. L. Fried, *J. Opt. Soc. Am.* **55**, 1427 (1965).
20. The factor by which the rms noise was reduced because of averaging by the control loop was estimated to be $\chi = [(2/\kappa) \tan^{-1}(\kappa/2)]^{1/2}$, where κ is the ratio of the sampling frequency to the control bandwidth (13).
21. Apart from the impact of finite laser spot size on

measurement error (negligible in our experiments because of the very high signal to noise ratio), anisoplanatism due to finite laser spot size [R. Sasiela, *Technical Report No. 807* (Lincoln Laboratory, Lexington, MA, 1988)] contributed a mean square error of $\sigma^2 = (0.1014\theta_{\text{gs}}/\theta_0)^{5/3} < 0.01$ for the parameters of our experiment, where $\theta_{\text{gs}} \sim 2 \text{ arc sec}$ is the laser spot size in the mesosphere and $\theta_0 = 3 \text{ to } 5 \text{ arc sec}$ is the isoplanatic angle. Hence, finite laser spot size was not a significant factor in our data.

22. This work was performed under the auspices of the U.S. Department of Energy by the LLNL under contract number W 7405-Eng-48.

28 April 1997; accepted 5 August 1997

Requirement for GD3 Ganglioside in CD95- and Ceramide-Induced Apoptosis

Ruggero De Maria, Luisa Lenti, Florence Malisan, Federica d'Agostino, Barbara Tomassini, Ann Zeuner, Maria Rita Rippo, Roberto Testi*

Gangliosides participate in development and tissue differentiation. Cross-linking of the apoptosis-inducing CD95 protein (also called Fas or APO-1) in lymphoid and myeloid tumor cells triggered GD3 ganglioside synthesis and transient accumulation. CD95-induced GD3 accumulation depended on integral receptor "death domains" and on activation of a family of cysteine proteases called caspases. Cell-permeating ceramides, which are potent inducers of apoptosis, also triggered GD3 synthesis. GD3 disrupted mitochondrial transmembrane potential ($\Delta\Psi_m$), and induced apoptosis, in a caspase-independent fashion. Transient overexpression of the GD3 synthase gene directly triggered apoptosis. Pharmacological inhibition of GD3 synthesis and exposure to GD3 synthase antisense oligodeoxynucleotides prevented CD95-induced apoptosis. Thus, GD3 ganglioside mediates the propagation of CD95-generated apoptotic signals in hematopoietic cells.

CD95 is a surface receptor that triggers apoptotic cell death when cross-linked by its specific ligand (1). This is mediated by the recruitment of different cytosolic proteins to the "death domain" of the receptor, an ~ 70 -amino acid protein-protein interaction domain that is essential for the generation of apoptotic signals. Seconds after the ligand induces the oligomerization of the receptor, the adaptor molecule FADD/MORT1 binds directly to the CD95 death domain, which in turn recruits caspase-8 (FLICE/MACH) (2). Other caspases then get activated in a proteolytic cascade, eventually leading to the hydrolysis of cytosolic and nuclear substrates (3).

Another pathway that depends on the death domain involves lipids and is also activated within 5 to 15 min after CD95

cross-linking (4): phosphatidylcholine-specific phospholipase C and acidic sphingomyelinase (ASM) are sequentially activated (5). Ceramides, generated from the hydrolysis of sphingomyelin by ASM, act as mediators of apoptosis in hematopoietic cells (6). Cells from individuals affected by Niemann-Pick disease, who are genetically deficient in ASM activity, or from mice in which the gene coding for ASM has been targeted, have defective apoptotic programs in response to radiation (7). However, the relevant targets of ceramides, or their metabolites, involved in downstream propagation of apoptotic signals remain poorly characterized. Newly synthesized or released ceramides are targeted to the Golgi complex and regulate sphingolipid and glycosphingolipid metabolism, including the rate of ganglioside biosynthesis within the Golgi (8). We therefore investigated whether changes in ganglioside metabolism could be detected during CD95 signaling.

Thin-layer chromatography (TLC) analysis of total cellular gangliosides revealed that when CD95 was cross-linked on HuT78, a cell line derived from a human

R. De Maria, F. Malisan, B. Tomassini, A. Zeuner, M. R. Rippo, R. Testi, Department of Experimental Medicine and Biochemical Sciences, University of Rome "Tor Vergata," 00133 Rome, Italy.

L. Lenti and F. d'Agostino, Department of Experimental Medicine and Pathology, University of Rome "La Sapienza," 00161 Rome, Italy.

*To whom correspondence should be addressed. E-mail: tesrob@flashnet.it