puesto que ésta estimula la actividad de AC mediante la inhibición de la proteína regulatoria inhibidora por la ribosilación por ADP de la subunidad alpha de la proteína Gi. Se utilizó toxina del cólera (CT) (10 ng/ml) por cuanto ésta activa en forma selectiva las proteínas G estimulantes. La actividad de AC fue determinada por la tasa de conversión de [α-^{32}P]ATP a cAMP en pmol/mg de proteína por 30 minutos. En 11 pacientes los niveles de AC estimulada por PT (8.55 ± 1.7) en los tejidos normales fueron superiores a los niveles basales de AC (5.14 ± 0.9, $p < 0.01$). Sin embargo, no se observó diferencia entre los niveles basales y los niveles estimulados por PT en los tejidos neoplásicos (6.43 ± 1.0 y 6.87 ± 1.8, respectivamente). Esto sugiere que existe menos proteína Gi en los neoplasmas puesto que la respuesta de AC a la PT fue mayor en un 170% en los tejidos normales y no se presentó estimulación significativa en los tejidos neoplásicos. En contraste, la respuesta de AC a la CT (10 μg/ml) que directamente activa las proteínas regulatorias guanil nucleotidas, fue mayor en el tejido neoplásico tiroideo (174.3 ± 30.1) que en el tejido tiroideo normal (78.5 ± 16.3) extraídos del mismo paciente ($p < 0.01$).

Estos experimentos demuestran que la mayoría de los neoplasmas tiroideos poseen menos proteína Gi y más proteína Ge, lo cual probablemente explica el mayor grado de respuesta de la AC a la TSH en los neoplasmas tiroideos. El mayor estímulo de Ge y el mayor grado de respuesta de la AC en los neoplasmas puede representar la razón del crecimiento más rápido de los tumores benignos y malignos de la tiroides.

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Invited Commentary

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More information is needed to understand the biologic behavior of differentiated thyroid carcinomas. Historically, a good prognosis has correlated with the patient's age, under 45 years, and smaller tumors without capsular or vascular invasion. A poorer prognosis is found in older patients with more extensive disease. To date, no single microscopic or ultrastructural feature has emerged as a reliable means of predicting a fatal outcome [1]. The extent of thyroidectomy as a determinant of outcome continues to be debated among experienced thyroid surgeons.

Clearly, there is a need for more basic knowledge on the mechanisms of growth in both benign and malignant thyroid neoplasms. Clark and co-workers continue to pursue this subject and their current report on regulatory proteins in thyroid

tissue is another fine example of their efforts. They found that thyroid neoplasms have less inhibiting guanyl nucleotide regulatory protein (Gi) and more stimulating guanyl nucleotide regulatory protein (Gs) when compared to normal thyroid tissue. The authors conclude that this altered ratio of regulatory proteins accounts for the greater adenylate cyclase response to thyroid stimulating hormone in thyroid neoplasms and may account for the more rapid growth of both benign and malignant thyroid neoplasms. While their methodology appears to be sound, the authors give no details in their report on the exact nature of the neoplastic thyroid tissue they studied nor any data on the difference between malignant and benign neoplastic tissue. The lack of specific data is a major weakness of this report. One would have to conclude that Clark and co-workers found no difference between benign and malignant neoplasms, which is, of course, disappointing. The authors should direct future efforts at detecting differences between thyroid neoplasms. Nonetheless, this report is significant in its relevance to the management of thyroid cancer since it sheds light on the possible mechanisms of tumor growth and TSH suppression by thyroid feeding.

The prognostic value of nuclear DNA content in patients with thyroid carcinomas is another area of intense study [2–4]. The presence of an increased DNA content when compared to a diploid cell is the basic definition of aneuploidy and is a well recognized feature of human cancer. A comparison of the ratio of regulatory proteins with nuclear DNA content appears to be a worthwhile area for future research. Such efforts would be facilitated by the development of monoclonal antibodies to both Gi and Gs proteins if flow cytometric DNA analysis is to be used.

If a consistent approach to the treatment of thyroid carcinomas is to emerge, then a clear understanding of the mechanisms of tumor growth is essential. More basic research, like that reported by Clark and colleagues, is the keystone of that effort.

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