region bridged by a disulfide bond. From this kininogen, bovine plasma kallikrein liberated two peptide fragments, in addition to bradykinin. One of the fragments was a biologically active histidine-rich peptide (fragment 2) consisting of 41 amino acid residues (Han et al., J. Biochem., 77, 55 (1975), and the other (fragment 1) was a glycopeptide containing also high level of histidine. The N-terminal sequence of Ser-Val-Gln-Val-Met-Lys-Thr-Glu-Gly--- of the glycopeptide was the same as C-terminal sequence of the CNBr-fragment involving kallidin (Komiya et al., J. Biochem., 76, 833 (1974)).
The release of these fragments in the course of digestion of HMW kininogen with plasma kallikrein was examined by SDS-polyacrylamide gel electrophoresis. At initial stage of the digestion, a large fragment was liberated in parallel with the release of bradykinin, producing kinin-free kininogen, and this large fragment was subsequently hydrolyzed into two fragments, histidine-rich peptide (fragment 2) and glycopeptide (fragment 1) mentioned above. These structural fragments derived from HMW kininogen were isolated preparatively and identified chemically. The kinin-free kininogen consisted of two chain polypeptides, heavy and light chains, which are held together by a disulfide bond.
On the digestions of HMW kininogen with other tissue kallikreins, they also liberated a few of peptide fragments, in addition to the kinin, but the chemical properties of these fragments seemed to slightly differ from those released by plasma kallikrein. As previously reported, LMW kininogen was resistant to the action of plasma kallikrein. On SDS-gel electrophoresis, no peptide grafments could be detected on the digest of LMW kininogen with plasma kallikrein. Comparison of the chimical structure of HMW and LMW kininogens will be also discussed.

ACCUMULATION OF MONONUCLEAR CELLS AND GROWTH-SLOWING OF SV-40 HAMSTER FIBROSARCOMAS FOLLOWING INTRA-TUMOR INJECTION OF BRADYKININ

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Two sites on male LSH inbred hamsters were injected with 10^5 male LSH SV-40 transformed fibrosarcoma cells. When the non-metastasizing subcutaneous tumors reached 10 mm diameter (at 5-5 1/2 weeks) tumors (one per hamster) were injected with 0.2 ml saline or bradykinin in 0.2 ml saline daily for four days and on days 5, 7, 10, 14, 18 and 21, with tumor diameters being measured daily prior to any injection. Animals with tumors reaching 10 mm diameter prior to or after 5-5 1/2 weeks were excluded for tumor growth kinetic comparison reasons. Splenic HDC activity was assayed by the 14-C

isotopic method of Schayer, and expressed as dpm per gram. Varying concentrations of bradykinin were used. One group received 50 micrograms per injection, another 250 μg.

By day 14 tumors on animals from the 250 μg bradykinin dose group were retarded in growth (6. 2± 0.7 S.E.M mm diameter increase) as compared with the saline-injected controls (16 ± 2.5 S.E.M. mm diameter increase). The 50 μg dose group was intermediate in growth rate between the control and the 250 μg group. Results are significant by value of less than ap.005 T-test. Splenic HDC the 250 μg bradykinin dose group was significantly elevated ($p = .05$) over the saline control group, (111,905 ± 23,000 dpm vs 49,597 ± 18.077 dpm), 8 hamsters per group. Normal hamster histidine decarboxylase levels were measured at 300,000 ± 95,000 dpm.

Histological study demonstrated no lymphocytic infiltration in non-injected tumor controls; saline-injected controls contained scattered lymphocytes, and bradykinin-injected tumors were massively infiltrated by mononuclear cells (with evidence of increased tumor cell destruction in these areas), as well as mononuclear cells in non-injected tumors on two-tumor bearing bradykinin injected animals. Second tumors on controls contained no lymphocytic infiltration. Non-injected tumors on two-tumor animals were not retarded in growth significantly despite accumulation of mononuclear cells.

These findings suggest a potential role for inter-related vasoactive substances (which act as mediators of inflammation) in the growth and development of neoplasms and possibly in the therapy of neoplasia.

ISOLATION OF PORCINE SUBMANDIBULAR KALLIKREIN

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Kallikrein from porcine submandibular glands was isolated by acetone precipitation, batchwise DEAE-sephadex adsorption, and affinity chromatography on trasylol-linked sepharose resin. Benzamidine was used to elute bound kallikrein from the resin. The specific activity of the purified kallikrein, assayed by the combined ADH/BAEE method, was 107.4 U/E280. When this kallikrein was subjected to disc gel electrophoresis at pH 8.9, only one band was observed. However, after treatment with SDS, disc gel electrophoresis gave one major band with 3 faster-running, less intense bands. Isoelectric focusing of the kallikrein on polyacrylamide gel discs gave an isoelectric point of 3.8 ± 0.2. This is similar to the isoelectric point 4.05/g pancreatic kallikrein B, measured on a sucrose-density gradient (Fiedler, Hirschauer and Werle, 1970).