During the past decade, the expression of growth factors and their receptors in tumours has attracted considerable attention. Cancer cells are postulated to escape from normal growth control by altered expression of growth factors, their receptors or intracellular signals. The discovery that many of these changes are associated with oncogene expression has been fundamental to the view that cancers result from the accumulation of multiple genetic insults. Although the roles of polypeptide growth factors, such as epidermal growth factor and platelet-derived growth factor have been widely discussed, neuropeptides have only recently been recognised as important mitogens (Hanley, 1985; Zachary et al., 1987). This review considers the evidence for neuropeptides as tumour growth factors.

Neuropeptides are small regulatory molecules that are widely distributed, particularly in the nervous and cardiovascular systems and gut. They can act as neurotransmitters and hormones. Many neuropeptides exist in multiple molecular forms, and different neuropeptides are frequently co-localised in neurones, suggesting complex modulation of their effects. Because of this, direct evidence of their actions cannot be obtained in vivo. Determination of the effects of individual peptides has only been possible since homogeneous cell lines were developed, such as murine Swiss 3T3 fibroblasts, which are reversibly growth arrested in serum-free medium.

Vasopressin was the first neuropeptide unequivocally shown to act as a growth factor (Rozen-gurt et al., 1979). The demonstration that bombesin, which was known to be secreted by small cell lung cancer (SCLC; Moody et al., 1981; Wood et al., 1981; Erisman et al., 1982) was also mitogenic (Rozen-gurt & Sinnett-Smith, 1983) focussed interest on neuropeptides as possible mediators of cancer growth. Because the bombesin-like peptides, including gastrin-releasing peptide (GRP), are the best characterised of the neuropeptide growth factors, their actions will be considered in detail. Evidence for other neuropeptides as growth factors, and their possible roles in malignant cells, will then be discussed.

**Bombesin/GRP**

GRP (27 amino acids) is the principal mammalian homologue of the amphibian peptide bombesin (14 amino acids). It is found in neurones of the gut and central nervous system, and is sparsely present in neuroendocrine cells of the adult lung. Vagal stimulation causes GRP release from the pancreas, and this stimulates the secretion of a variety of hormones including gastrin, leading to gastric acid and amylase secretion.

Bombesin/GRP is a potent mitogen for Swiss 3T3 cells. It is active in the absence of other growth factors (with half-maximal effect at 1 nM) but synergises with insulin (Rozen-gurt & Sinnett-Smith, 1983). Bombesin/GRP has been reported to be mitogenic for explants of human bronchial epithelium at concentrations of 100 nM (Willey et al., 1984). Because GRP is abundant in fetal lung, it has been suggested to act as a developmental growth factor (Wharton et al., 1978; Spindel et al., 1987). Indirect evidence that bombesin can act as a growth factor in vivo has been obtained in rodents, in which chronic bombesin administration leads to gastric antral cell proliferation and pancreatic hypertrophy (Lecoche et al., 1981; Lehy et al., 1983; Lhoste et al., 1989).

Bombesin/GRP is found in specimens and cell lines of SCLC, and also in some bronchogenic adenocarcinomas (Moody et al., 1981; Wood et al., 1981; Erisman et al., 1982). The mRNA for GRP has been detected in SCLC and correlates well with immunoreactive GRP (Suzuki et al., 1987). GRP receptors have been demonstrated on SCLC cells (Moody et al., 1985a; Layton et al., 1988) and GRP has been shown to stimulate SCLC growth in vitro and in vivo at concentrations of 50 nM–1.8 μM (Weber et al., 1985; Carney et al., 1987; Alexander et al., 1988). Thus the components required for autocrine growth stimulation are present, although the lack of correlation between amounts of GRP secreted, response to exogenous GRP and number of binding sites is disappointing (Carney et al., 1987). The autocrine hypothesis was tested by Cutitita et al. (1985) using a monoclonal antibody to bombesin. The clonal growth of two SCLC lines was inhibited in vitro, as was the growth of medullary thyroid carcinomas (Spindel et al., 1984; Bostwick & Bensch, 1985). In addition bombesin/GRP has been found to have effects (although not necessarily of growth promotion) in hormone-dependent tumours of prostate and breast (Bologna et al., 1989; Weber et al., 1989; Giachetti et al., 1990; Patel & Schrey, 1990). Bombesin has also been implicated in the development of some carcinogen-induced pancreatic and hepatocellular tumours in rats (Lhoste & Longnecker, 1987; Seglen et al., 1989).

Although interest in GRP as a tumour growth factor has been concentrated on SCLC, it is detectable in other neuroendocrine tumours such as carcinoids and medullary thyroid carcinomas (Spindel et al., 1984; Bostwick & Bensch, 1985). In addition bombesin/GRP has been found to have effects (although not necessarily of growth promotion) in hormone-dependent tumours of prostate and breast (Bologna et al., 1989; Weber et al., 1989; Giachetti et al., 1990; Patel & Schrey, 1990). Bombesin has also been implicated in the development of some carcinogen-induced pancreatic and hepatocellular tumours in rats (Lhoste & Longnecker, 1987; Seglen et al., 1989).

**Mode of action**

Bombesin/GRP was first shown to be mitogenic in Swiss 3T3 cells, and much work elucidating its signal transduction pathways has been done in these cells (Rozen-gurt, 1986). GRP binds to a single class of high affinity receptors of M, 75,000–85,000 (Zachary & Rozen-gurt, 1985; 1987; Kris et al., 1987). These are glycoproteins with a core of M, 42,000, which are associated with a guanine nucleotide binding protein (G-protein; Sinnett-Smith et al., 1990; Coffer et al., 1990). They have now been shown to be members of the G-protein coupled receptor super-family, with seven predicted transmembrane domains (Battey et al., 1991) like the receptor for substance K (see below).

Binding of bombesin/GRP to its receptor triggers a cascade of signals in the membrane, cytosol and nucleus leading to DNA synthesis 10–15 h later. One of the earliest changes is a rapid exchange of Na+, H+ and K+ ions across the cell membrane, which leads to cytoplasmatic alkalisation and an...
increase in intracellular \([K^+]\) (Mendoza et al., 1986). Bombesin/GRP also stimulates phospholipase C-mediated hydrolysis of phosphatidyl-4,5-bisphosphate in the plasma membrane, generating diacylglycerol and inositol-1,4,5-trisphosphate, which causes rapid mobilisation of \(Ca^{2+}\) from intracellular stores (Mendoza et al., 1986; Takuwa et al., 1987). The diacylglycerol thus produced activates protein kinase C, leading to phosphorylation of its M, 80,000 sub- 

late in the stomach (Hoosein et al., 1990). Surgical intervention associated with development of gastrin-secreting tumours (Mendoza et al., 1986; Takuwa et al., 1987). The diacylglycerol thus produced activates protein kinase C, leading to phosphorylation of its M, 80,000 sub-

strate protein (Rozengurt et al., 1983; Isacke et al., 1986; Zachary et al., 1986). Bombesin/GRP is a potent mitogen which is active alone, and demonstrates considerable redundancy in its signalling pathways: accumulation of cAMP and prostaglandins have recently been demonstrated to be impor-
tant in other mammalian (Millar & Rozengurt, 1988, 1990). Like PDGF and other growth factors, bombesin/GRP rapidly and transiently induces expression of the oncogenes c-fos and c-myc (Letterio et al., 1986; Rozengurt & Sinnett-Smith, 1988). As these cellular oncogenes encode nuclear proteins, it is plausible that their expression plays a part in the transduction of the mitogenic signal to the nucleus.

Available evidence suggests that the effects of bombesin/GRP in SCLC resemble those in Swiss 3T3 cells. 11\(\beta\)-GRP binds to specific cell surface receptors on SCLC cell lines (Moody et al., 1985a; Layton et al., 1988) and stimulation with bombesin/GRP causes rapid and transient mobilisation of intracellular \(Ca^{2+}\) (Heikkila et al., 1987; Moody et al., 1987) with inositol phosphate turnover (Trepel et al., 1988). The finding that neuropeptide antagonists characterised in Swiss 3T3 cells can block receptor-mediated events in SCLC strengthens the predictive value of the fibroblast model (Woll & Rozengurt, 1990).

**Gastrin**

This 17 amino acid peptide is localised to neurones of the hypothalamus and pituitary, and neuroendocrine cells of the gastric antrum and proximal duodenum. Gastrin release stimulates gastric acid secretion, gastric motility and contraction of the lower oesophageal sphincter. The receptors and signalling pathways remain obscure.

Considerable indirect evidence indicates that gastrin has trophic effects on the normal pancreas and gastrointestinal mucosa *in vivo*. Exogenous gastrin stimulates DNA synthesis in the fundic gastric mucosa and an increase in pancreatic weight (Hansen et al., 1976; Solomon et al., 1987; Ryberg et al., 1990). Surgical antrectomy in the rat leads to reduced DNA synthesis in the pancreas, oesophagogastric, duodenal and colonic mucosa that can be reversed with pentagastrin treatment (Dembinski & Johnson, 1979). It also impairs the proliferative response to partial hepatectomy (Rasmussen et al., 1990).

Persistent elevation of plasma gastrin in rats treated with \(H_2\) antagonists and omeprazole has been associated with the development of gastric carcinoid tumours (Ekman et al., 1985; Poynter et al., 1985; Betton et al., 1988). In contrast, gastrin-secreting tumours in man (gastrinomas) are associated with peptic ulcers and diarrhoea, but not with gastric carcinoids. Gastrin has also been implicated in the pathogenesis of some gastric and colonic adenocarcinomas (Lamers & Jansen, 1988). Plasma gastrin levels are higher in patients with colonic polyps or cancer than in control subjects (Smith et al., 1989) but interestingly, the presence of gastrin receptors on colonic cancers is associated with a good prognosis (Upp et al., 1989). Gastrin stimulates the growth of rat gastric cancer cells *in vitro* (Kobori et al., 1982) and of gastric and colonic tumour xenografts in nude mice, apparent- 

ly through specific receptors (Sumiyoshi et al., 1984; Singh et al., 1986; Watson et al., 1989). Preliminary studies with gastrin antagonists and antibodies have shown growth retardation of colon cancer cell lines and suggest that colon tumours can be stimulated by gastrin in an autocrine fashion (Hoosein et al., 1988, 1990). Gastrin has also been found in some bronchogenic tumours (Gazdar & Carney, 1984; Rehfeld et al., 1989).

**Cholecystokinin**

Multiple molecular forms of cholecystokinin are found, but the biological activity resides in the conserved eighth carboxy-
terminal amino acids. It is localised to the proximal small intestine, ileum, cerebral cortex, hypothalamus and brainstem. Its main effects in the gut are to stimulate gall bladder contraction and secretion, but its central actions probably mediate pain and satiety.

Cholecystokinin has trophic effects on normal pancreas, as shown by measurements of pancreatic weight and DNA syn-
thesis (Haarstad et al., 1986; Douglas et al., 1989). It can also directly stimulate the growth of rat gastric cancer cells *in vitro* (Kobori et al., 1982) and has been implicated in the growth of gut tumours (Lammers & Jansen, 1988; Hoosein et al., 1990). Cholecystokinin has been demonstrated in a liver metastasis from an islet cell tumour (Madsen et al., 1986), pituitary tumours (Rehfeld et al., 1987) and some SCLC (Gazdar & Carney, 1984; Rehfeld et al., 1989). Cholecystokinin receptors have been found in some SCLC (Yoder & Moody, 1987) and shown to mobilise \(Ca^{2+}\) in SCLC cell lines (Staley et al., 1989a; Woll & Rozengurt, 1989a; Bunn et al., 1990), suggesting a possible role as growth factors for a subset of these tumours.

**Neurotensin**

This 13 amino acid peptide is found principally in the central nervous system, pituitary gland and gut. Its functions are unclear, but intracerebral injection is known to cause hypotension, hypothermia and hypoglycaemia, in addition to release of pituitary hormones.

Neurotensin is produced by some SCLC (Wood et al., 1981; Goedert et al., 1984; Moody et al., 1985b). \(Ca^{2+}\)-mobilising receptors for it have recently been demonstrated on SCLC cell lines (Staley et al., 1989b; Woll & Rozengurt, 1989a; Bunn et al., 1990). The finding that exogenous neurotensin can stimulate SCLC growth suggests that it may act as an autocrine growth factor for this tumour (Davis et al., 1989).

**Vasopressin**

Vasopressin (antidiuretic hormone) is a cyclic nonapeptide which is secreted in the hypothalamus and passes down neural axons to the posterior pituitary where it is released into the circulation. Acting as an endocrine hormone, it stimulates hepatic glycogenolysis and has pressor effects on arteriolar smooth muscle, mediated by \(Ca^{2+}\)-mobilising V1 receptors. It also has antidiuretic effects mediated by adenylyl cyclase-coupled V2 receptors in the kidney. As yet, the molecular structures of the vasopressin receptors are unknown.

Direct evidence for the mitogenic effects of vasopressin was first obtained in Swiss 3T3 cells (Rozengurt et al., 1979). It acts synergistically with insulin at nanomolar concentrations. Vasopressin binds to specific, high-affinity V1 receptors in these cells (Collins & Rozengurt, 1983) and elicits an array of early responses including inositol phosphate production, \(Ca^{2+}\)-mobilisation, cytoplasmic alkalisation, activation of protein kinase C and oncogene induction (Rodriguez-Pena & Rozengurt, 1986; Lopez-Rivas et al., 1987; Rozengurt & Sinnett-Smith, 1988). In vivo, vasopressin facilitates the proliferative responses to haemorrhage (Hunt et al., 1977; Feuerstein et al., 1985) and partial hepatectomy (Russell & Bucher, 1983) in rats. It has also been implicated in the control of brain development in fetal rats (Boer, 1985).

Vasopressin has not been shown to be mitogenic for tumours. It is, however, secreted (with other neurophysins) by up to 65% of SCLC (1982) and has been implicated in viral (Russell & Bucher, 1983) in rats. It has also been implicated in the control of brain development in fetal rats (Boer, 1985).

Vasopressin secretion is more com-
Tachykinins

The tachykinins, including substance P (11 amino acids) and substance K (ten amino acids), have similar activities but bind to distinct receptors. They are widely distributed in the brain, spinal cord and gut neurons. Their release causes local pain, smooth muscle contraction and vasodilation, in addition to their systemic effects of stimulating natriuresis and salivation, and inhibiting pancreatic and biliary secretion. The substance K receptor was the first neuropeptide receptor to be cloned and sequenced (Masu et al., 1987). The substance P receptor has considerable homology with it (Yokota et al., 1989; Hershey & Krause, 1990). They are members of a group of receptors characterised by having seven helical transmembrane domains, clustered to form a ligand-binding pocket, and coupled to Ca²⁺-mobilising G-proteins (Dohlan et al., 1987; Lefkowitz & Caron, 1988).

Substance P has been shown to have direct mitogenic effects on T-lymphocytes, mediated by specific receptors, at concentrations as low as 100 pM (Payan et al., 1983). Tachykinins can also stimulate growth of human skin fibroblasts, arterial smooth muscle cells and keratinocytes (Nilsson et al., 1985; Tanaka et al., 1988). These, and earlier observations in vivo, have led to speculation that tachykinins mediate inflammation and wound healing (Payan, 1989). Substance P receptors are expressed in healing glia following nerve injury and in normal brain (Tantykh et al., 1989). Tachykinins have also been implicated in the pathogenesis of rheumatoid arthritis, as substance P stimulates prostaglandin E2 release and proliferation of synoviocytes (Lotz et al., 1987).

Tachykinins are not known to be tumour growth factors, but they are secreted by some carcinoid tumours (Norheim et al., 1986; Bishop et al., 1989). The tachykinins have been demonstrated to mobilise Ca²⁺ in SCLC cell lines, but not to stimulate growth (Takura et al., 1990). An amphibian tachykinin, physalaemin (11 amino acids), is produced by some SCLC and appears to be able to inhibit SCLC growth, suggesting a possible regulatory role in this cancer (Lazarus et al., 1983; Bepler et al., 1987).

Bradykinin

The nonapeptide bradykinin is generated in the plasma or tissues from high molecular weight precursors (kinogens) by the action of kallikreins, which are activated during proteolysis and clotting. It is rapidly degraded, so plasma concentrations are very low. Bradykinin is implicated in smooth muscle contraction, vasodilation and vascular permeability. It is one of the most potent pain producing substances known, and its receptors are localised to the nociceptive sensory pathways (Steranka et al., 1988). Bradykinin is a weak mitogen for human fibroblasts (Owen & Villereal, 1983; Coughlin et al., 1985) but a potent mitogen for Swiss 3T3 cells (Woll & Rozengurt, 1988a). Acting synergistically with insulin in these cells, nanomolar concentrations of bradykinin achieve a response equivalent to that obtained with serum. Although bradykinin receptor subtypes can be discriminated pharmacologically, these do not correlate with functional differences, and the structures of the receptors are unknown. Bradykinin induces monovalent ion fluxes, transient protein kinase C activation, inositol phosphate production, Ca²⁺-mobilisation, prostaglandin E₂ production and myc induction (Owen & Villereal, 1983; Coughlin et al., 1985; Jackson et al., 1987; Issandou & Rozengurt, 1990).

Bradykinin has not been demonstrated to act as a tumour growth factor. Its production however, has long been associated with the flushing caused by carcinoid tumours, which can secrete large quantities of vasoactive peptides (Oates et al., 1984; Gustafsen et al., 1987). Interestingly, [hydroxyproplyl]-bradykinin has been detected in the ascitic fluid of a patient with gastric cancer (Maeda et al., 1988). Bradykinin has now been shown to stimulate Ca²⁺ mobilisation in SCLC cell lines (Woll & Rozengurt, 1989a; 1990). Because it is produced at sites of tissue damage and rapidly inactivated, it could have local effects within tumours without being detected in serum by current assay methods.

Opioids

Endogenous opioid peptides including the enkephalins, endorphins and dynorphins are widely distributed in the central nervous system. Multiple subtypes of receptors have been identified using a variety of agonists and antagonists. Because of their central role in pain transmission, opiate pharmacology has been studied in detail.

β-endorphin stimulates lymphocyte proliferation in vitro, although this effect may not be mediated directly by opiate receptors as it is not blocked by the opiate antagonist nal-tetrazine (Gilman et al., 1982). Dynorphins and enkephalins appear to be involved with vasopressin in the proliferative response of the rat marrow to haemorrhage (Feuerstein et al., 1985). Further, β-endorphin has been implicated in the ability of newts to regenerate amputated limbs (Morley & Ensor, 1986).

SCLC cell lines contain opioid peptides and receptors (Roth & Barchas, 1985). Opioids have been reported both to inhibit and to stimulate SCLC growth (Davis et al., 1989; Maneckjee & Minna, 1990). Opioids are also reported to inhibit the growth of breast cancer cells (Maneckjee et al., 1990). Conversely, neuroblastoma xenograft growth can be inhibited by naltrexone (Zagon & McLaughlin, 1987), a reminder of the complex interactions between multifunctional growth factors (Sporn & Roberts, 1988).

Vasoactive intestinal peptide (VIP)

This 28 amino acid peptide is found in large amounts in mammalian brain, and in gut mucosa and muscle, where it is localised to postganglionic nerves. It is also found in the salivary glands, pancreas, respiratory and urogenital tracts. Neural stimulation causes release of VIP, which binds to specific receptors. These receptors also bind related hormones (e.g. secretin, glucagon) with lower affinity. VIP induces relaxation of smooth muscle, vasodilation and enhanced small intestinal and colonic secretion.

In Swiss 3T3 cells, VIP stimulates mitogenesis in the presence of insulin and cAMP phosphodiesterase inhibitors. In contrast to bombesin, vasopressin and bradykinin, VIP is a weak mitogen for these cells, and its effects are mediated by elevation of cAMP without Ca²⁺-mobilisation or protein kinase C activation (Zurier et al., 1988). VIP also stimulates adenylate cyclase activity and cell proliferation in keratinocytes (Haegerstrand et al., 1989).

VIP has been found in pancreatic, neural and cervical tumours and phaeochromocytomas (Bunnett et al., 1984; Inoue et al., 1984; Viale et al., 1985), but is not known to be a growth factor for them. Pancreatic and intestinal VIP-secreting tumours (vipomas) present with the Verner-Morrison syndrome of watery diarrhoea, hypokalaemia and achlorhydria. Interestingly, this syndrome, and elevated VIP levels, were recently reported in a patient with SCLC (Noseda et al., 1989). Some SCLC appear to have binding sites for VIP and VIP can stimulate growth of certain SCLC cell lines in vitro. This effect could be mediated by bombesin because exogenous VIP stimulates bombesin/GRP secretion (Bepler et al., 1988).
Further neuropeptide growth factors

The number of neuropeptides shown to be mitogenic is rapidly increasing. Serotonin (5-hydroxytryptamine) has long been known to be a component of the carcinoid flush and is also secreted by some SCLC (Horai et al., 1973; Matsuo, 1988). Its receptor has been cloned and belongs to the class of G-protein linked receptors with seven helical transmembrane domains (Julius et al., 1988). Expression of the serotonin receptor in fibroblasts leads to malignant transformation, suggesting that it can act as a proto-oncogene (Julius et al., 1989). Whether this is significant in any human cancer is unknown. The angiotensin receptor, which has a similar structure, is also encoded by an oncogene, mas (Youn et al., 1986; Jackson et al., 1988).

The recently described neuropeptide endothelin, and related vasoconstrictor peptides, stimulate DNA synthesis by a Ca²⁺ dependent pathway in a variety of cell types including fibroblasts, smooth muscle and glial cells (Komuro et al., 1988; Yanigasawa et al., 1988; Takau et al., 1989; Fabregat & Rozengurt, 1990). Endothelin is produced by breast, pancreas and colon cancer cell lines, but it is not yet known whether these, or surrounding stromal cells, are stimulated by it (Kusuhara et al., 1990).

Therapeutic implications

The recognition that many neuropeptides can act as growth factors, the identification of these peptides and their receptors in human cancers, and the discovery that some are encoded by oncogenes (Young et al., 1986; Jackson et al., 1988; Julius et al., 1989), have led to speculation that neuropeptides are important regulators of tumor growth. It has long been known that tumors can secrete diverse peptides, in a heterogeneous fashion. Only recently however have multiple receptors been demonstrated on cancer cells, prompting the suggestion that growth of these tumors is regulated by multiple factors acting in a paracrine or autocrine manner (Woll & Rozengurt, 1989a).

SCLC is the best example of this model. It can secrete a wide variety of ectopic peptides and hormones (Table 1). Many of these have been shown to act as growth factors for other cell types, in vitro and in vivo. The demonstration of receptors for bombesin/GRP, bradykinin, cholecystokinin, galanin, gastrin, neurotensin, tachykinins and vasopressin on SCLC permits speculation that these diverse peptides may contribute to multiple growth loops. Direct evidence of growth stimulation in SCLC is at present available only for bombesin/GRP, neurotensin and β-endorphin, but it is likely that further neuropeptide mitogens will soon be added to this list. Other tumours for which neuropeptide growth factors may be important include the neuroendocrine cancers (e.g. carcinoids, medullary carcinoma of thyroid) and adenocarcinomas of stomach, colon, breast and prostate.

The model proposed, of tumour growth regulation by multiple neuropeptide growth factors, has implications for future therapeutic strategies. Attempts to produce highly specific antibodies and antagonists to these growth factors are unlikely to be successful except in a minority of cases. At best, 30–60% of cells may express receptors for any individual peptide (Bunn et al., 1990) but all or most tumours will express receptors for multiple peptides (Woll & Rozengurt, 1989a). Possible strategies to exploit this knowledge include targeting a signalling process common to the diverse peptides, attacking an enzyme essential to growth factor production, and developing broad-spectrum receptor antagonists. Elucidation of mitogenic signalling pathways has identified a number of intracellular messengers used by many mitogens, such as protein kinase C activation or ion fluxes, that could be targets for novel therapies (Woll & Rozengurt, 1989b). Broad-spectrum neuropeptide antagonists, that appear to act on a class of G-protein-linked, Ca²⁺-mobilising receptors, have already been shown to block the early events stimulated by diverse neuropeptides and to inhibit SCLC growth in vitro (Woll & Rozengurt, 1989b, 1990). Increasing knowledge of the actions of neuropeptide growth factors in tumours will undoubtedly lead to innovations in cancer treatment.

Table 1 Peptides and hormones secreted by SCLC

| Peptide                          | Receptor | Functions |
|---------------------------------|----------|-----------|
| Adrenocorticotrophin            | Lipotropin|           |
| Atrial natriuretic peptide      | Neuropeptin|          |
| Bombesin/GRP                    | Opioid peptides|       |
| Calcitonin                      | Oxytocin |           |
| Calcitonin gene related peptide | Parathyroid hormone|     |
| Cholecystokinin                 | Physalaem |          |
| Chorionic gonadotrophin         | Prolactin |           |
| Estradiol                       | Serotonin |           |
| Follicle stimulating hormone    | Somatostatin|         |
| Gastrin                         | Substance K|         |
| Glucagon                        | Substance P |          |
| Granulocyte colony stimulating factor | Transferrin |      |
| Growth hormone                  | Vasopressin|           |
| Growth hormone releasing factor | VIP       |           |
| Insulin-like growth factor-1    |          |           |

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Opioid peptides

Neuropeptide

Parathyroid hormone

Physalaemin

Prolactin

Serotonin

Somatostatin

Substance K

Substance P

Transferrin

Vasopressin

VIP
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